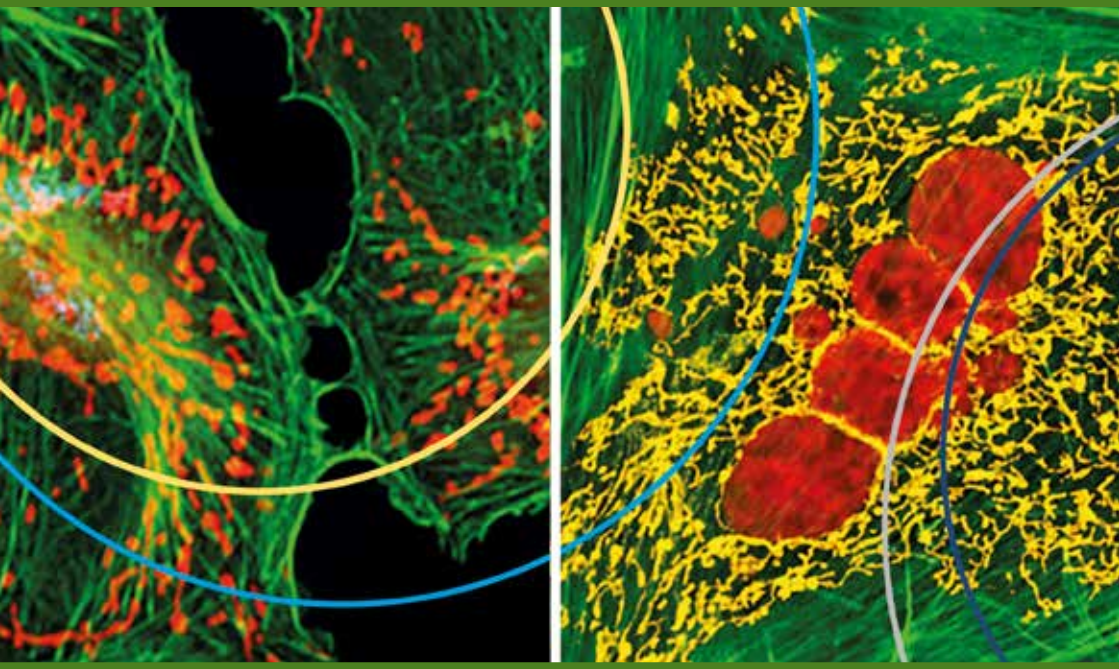
BOOK OF ABSTRACTS



Cell Physics 2017

11.-13. Oktober 2017
Saarbrücken

SFB 1027 DFG INM alvéole TAKE CARE OF YOUR CELLS UNIVERSITÄT DES SAARLANDES

Welcome...

...to the conference "Cell Physics 2017" at the Saarland University in Saarbrücken, Germany, 11.-13.10.2017. The conference is organized and Ginanced by the Collaborative Research Center *SFB 1027* "Physical modeling of non-equilibrium processes in biological systems". It is intended to be an interdisciplinary platform for scientific exchange between participants from cell biology and biophysics, both represented in roughly equal numbers, and focusses centrally on theoretical concepts in conjunction with cell biological experiments. Topics include

- Cell Mechanics and Adhesion
- Cytoskeleton Dynamics
- Membrane Proteins
- Biofilm Formation
- Tissue Growth
- Physics of Cancer

The conference will start Wednesday 11.10.2017 at 9:00 am, and finish Friday, 13.10.2017 at 3:30 pm. It consists of invited talks, contributed oral presentations and poster sessions.

Heiko Rieger, Ludger Santen (Saarland University, Germany)

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UNIVERSITÄT DES SAARLANDES

Cell Physics 2017

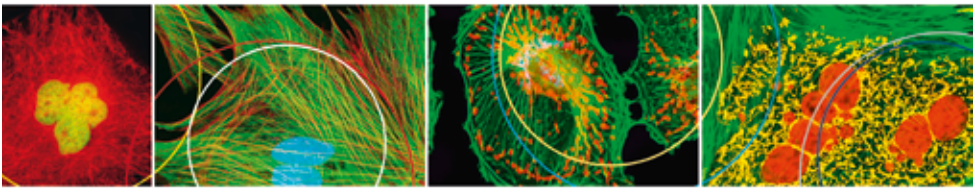
11. - 13. Oktober | Saarbrücken

TOPICS

Cell Mechanics and Adhesion
Cytoskeleton Dynamics
Membrane Proteins
Biofilm Formation
Tissue Growth
Physics of Cancer

INVITED SPEAKERS

Marino Arroyo (Polytech. Univ. of Catalonia, Barcelona, Spain)
Daniel Bonn (University of Amsterdam, Netherlands)
Lorenzo Cingolani (Italian Institute for Technology, Italy)
Yves Dufrêne (University of Leuven, Belgium)
Rudi Ettrich (Center f. Nanobiol. & Structural Biol., Czechia)
Ben Fabry (University of Erlangen-Nürnberg, Germany)
Maike Glitsch (University of Oxford, UK)
Robert Grosse (Biochem.-Pharmacol. Center Marburg, Germany)
Jochen Guck (Technical University Dresden, Germany)
Sarah Köster (University of Göttingen, Germany)
Jane Kondev (Brandeis University, USA)
Caterina la Porta (University of Milano, Italy)
Frederick MacKintosh (Rice University, USA)
Berenike Maier (University of Cologne, Germany)
Sergi Garcia Manyes (Kings College London, UK)
Francois Nedelec (EMBL Heidelberg, Germany)
Raz Palty (Technion Haifa, Israel)
Felix Ritort (University of Barcelona, Spain)
Pere Roca-Cusachs (Inst. f. Bioeng. of Catalonia, Barcelona, Spain)
Ulrich Schwarz (University of Heidelberg, Germany)
Gasper Tkacik (Institute of Science and Technolgy, Austria)
Xavier Trepat (Inst. f. Bioeng. of Catalonia, Barcelona, Spain)
Katarina Wolf (Inst. f. Molecular Life Sciences, Netherlands)
Ronen Zaidel-Bar (National University of Singapore)
Stefano Zapperi (University of Milano, Italy)



ORGANIZERS (UdS)

Heiko Rieger
Ludger Santen

http://www.cell-physics.uni-saarland.de

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Conference Program

Wednesday 11.10.2017			
08.45 - 09.00	Opening		
09.00 - 10.30		**Cytoskeleton I**	
09.00 - 09.30	Ben Fabry	Forces and cytoskeletal dynamics during collective invasion of tumor spheroids	I.6
09.30 - 10.00	Sarah Köster	Cytoskeletal Intermediate Filaments –from Self-Assembly to Cell Mechanics	I.12
10.00 - 10.30	Marino Arroyo	Sub- and supra-cellular mechanisms of tension buffering	I.1
10.30 - 11.00	**Coffee-Break**		
11.00 - 12.30		**Orai / Calcium**	
11.00 - 11.30	Raz Palty	A molecular mechanism for Orai1 channel activation by STIM1	I.17
11.30 - 12.00	Rudi Ettrich	Modulation of human ORAI1 channels: modeling and simulations	I.5
12.00 - 12.30	Maike Glitsch	Environmental stiffness regulates intracellular Ca2+ signals through the proton-sensing receptor OGR1	I.8
12.30 - 14.00	**Lunch**		
14.00 - 15.30		**Active Matter**	
14.00 - 14.30	Fred MacKintosh	Phase Transitions, Non-equilibrium Fluctuations and Broken Detailed Balance in Biological Systems	I.14
14.30 - 15.00	Felix Ritort	Physical and biological aging of red blood cells	I.18
15.00 - 15.30	Daniel Bonn	Porosity Governs Mechanical Properties of Biopolymer Gels	I.2
15.30 - 16.00	**Coffee Break**		

	Conference Building E2 2		*Conference Building E2 5*	
16:00-17:30	**Cell Mechanics I**		**Cytoskeleton**	
16.00-16.15	Jaume Casademunt	Active wetting of epithelial tissues C.5	Jan Kierfeld	Microtubule tug-of-war and stochastic kinetochore oscillations C.22
16.15-16.30	Carles Blanch-Mercader	Hydrodynamic instabilities, waves and turbulence in spreading epithelia C.3	Jan Brugués	Autocatalytic microtubule nucleation determines the size and mass of spindles C.4

16.30-16.45	Danielle Holz	Cell Protrusion and Retraction Driven by Fluctuations in Actin Polymerization: A Two-Dimensional Mathematical Model C.17	Alexandr Nasedkin	Essential dynamics of tubulin in a microtubular fragment C.26
16.45-17.00	Ricard Alert	Bleb nucleation through membrane peeling C.2	Sushil Dubey	Mechanical responses of axonal cytoskeleton C.11
17.00-17.15	Sebastian Hillringhaus	The Mechanics of Vesicle Blebbing C.15	Brandon G. Horan	Multiscale Model of the Formin Homology 1 Domain Illustrates its Role in Regulation of Actin Polymerization C.18
17.15-17.30	Chii Jou Chan	Organ size control via the interplay between luminal pressure and cell mechanics C.6	Anne E. Hafner	Spatial cytoskeleton organization supports targeted intracellular transport C.14
17.30 - 19.00		**Poster - Session I**		
19.00		**Dinner**		

Thursday 12.10.2017			
09.00 - 10.30		**Cell Mechanics I**	
09.00 - 09.30	Jochen Guck	Biophysical techniques for the study of phase transitions in cells	I.10
09.30 - 10.00	Yves F. Dufrêne	Force nanoscopy in microbiology	I.4
10.00 - 10.15	Karin Jacobs	Exploring the basic mechanisms of bacterial contact formation and breaking: Combining AFM force spectroscopy & MC simulations	C.21
10.15 - 10.45	Berenike Maier	Correlating bacterial interaction forces with biofilm structure	I.15
10.45 - 11.00	**Coffee-Break**		
11.00 - 12.30		**Nucleus**	
11.00 - 11.30	Jane Kondev	Action at a Distance in the Yeast Nucleus	I.11
11.30 - 12.00	Katarina Wolf	Control of cancer cell invasion by nuclear deformability	I.23
12.00 - 12.30	Pere Roca-Cusachs	Force triggers YAP nuclear entry by mechanically regulating transport across nuclear pores	I.19
12.30 - 14.00	**Lunch**		
14.00 - 15.30		**Cytoskeleton II**	
14.00 - 14.30	Francois Nedelec	Cytoskeletal Mechanics of Blood Platelets	I.16
14.30 - 15.00	Robert Grosse	Actin as an intranuclear force generator?	I.9
15.00 - 15.30	Ronen Zaidel-Bar	Regulation of actomyosin contractility: lessons from C. elegans	I.24
15.30 - 16.00	**Coffee Break**		

16:00-17:30	*Conference Building E2 2* **Cell Mechanics II**		*Conference Building E2 5* **Proteins / Genes**	
16.00-16.15	Dimitry Fedosov	What can we learn from the observation of red blood cell membrane fickering? C.12	Saroj Kumar Nandi	Protein gradients in single cells induced by “morphogen”-like diffusion C.25
16.15-16.30	Ohad Cohen	Non-Linear dynamics of beating cardiomyocytes C.7	Indra Navina Dahmke	Graphene liquid -enclosure facilitates single protein analysis in whole cells by electron microscopy C.8
16.30-16.45	Dan Deviri	Rupture dynamics and chromatin loss in deformed nuclei C.10	Niels de Jonge	Analysis of ion channel stoichiometry within single cells via liquid-phase electron microscopy and modeling C.9
16.45-17.00	Nils Klughammer	Flows in Starfss Oocyte Cytoplasm Driven by Surface Contraction Wave C.23	Stefan Gahbauer	Homo- and Heterodimerization of G protein coupled Chemokine receptors C.13

17.00-17.15	Shrikrishnan Sankaran	Optogenetically regulated biomaterials: novel microenvironments for studies in mechanotransduction C.28	Wasnik Vaibhav	Positional information readout in Ca^{2+} signaling C.31
17.15-17.30	Shayan Shamipour	Cytoplasmic actomyosin contractions drive streaming in zebrafss eggs C.29	Thomas Sokolowski	Deriving the Drosophila gap gene system ab initio by optimizing information flow C.30

17.30 - 19.00 Poster - Session II

Friday 13.10.2017			
09.00 - 10.45		**Cell Mechanics II**	
09.00 - 09.30	Ulrich Schwarz	Emergence of elasticity in adherent cells	I.20
09.30 - 10.00	Xavier Trepat	Physical forces driving migration, division and folding of epithelial sheets	I.22
10.00 - 10.45	Caterina La Porta and Stefano Zapperi	Tackling cell deformation, division and migration by a combination of experiments and computational models	I.25
10.45 - 11.15	**Coffee-Break**		

11.15-12.30	*Conference Building E2 2* **Adhesion**		*Conference Building E2 5* **Cancer / films**	
11.15-11.30	Linda Hofherr	Adhesion forces of spherical bacteria investigated by scanning force microscopy C.16	Edoardo Milotti	Tumor phenomenology in cell-based computer simulations C.24
11.30-11.45	Katharina Huttenlochner	Forces for lateral detachment of bacterial cells from structured component surfaces C.19	Shengnan Xiang	Altering nanoparticle uptake pathway by engineering cell membrane stiffness C.33
11.45-12.00	Jagoba Iturri	Atomic Force Microscopy as a precision tool to study cell mechanics and adhesion C.20	Guglielmo Saggiorato	Propagation of dipoles in non-linear elastic media C.27
12.00-12.15	Maria Akhmanova	Modeling of epithelial sheet deformation under external force applied by a migrating cel C.1	Doriane Vesperini	A microfluidic method for ca psule and cell sorting based on mechanical properties C.32
12.15-12.30			Yong Liu	Influence of vinegar on biofilms formation in situ C.34
12.30 - 14.00	**Lunch**			

14.00 - 15.30		**Proteins / Genes**	
14.00 - 14.30	Sergi Garcia-Manyes	Linking mechanochemistry with protein folding with single bond resolution	I.7
14.30 - 15.00	Lorenzo Cingolani	Integrins in synaptic excitability: relevance for neurodevelopmental disorders	I.3
15.00 - 15.30	Gasper Tkacik	Optimal decoding of cellular identities in a genetic network	I.21
15.30	**Closing / Poster Awards**		

Poster List

P1	Arita, Chikashi	Bidirectional Non-Markovian Exclusion Processes
P2	Barberi, Luca	On the growth of helical pipe protrusions out of lipid bilayers interacting with ESCRT-III subunits
P3	Basu, Saikat	Substrate stiffness differentially alters cell proliferation and apoptosis during tissue morphogenesis
P4	Becker, Björn	Novel roles of KDEL receptor at the cell surface of mammalian and yeast cells
P5	Böckmann, Rainer	Transmembrane Protein-Induced Membrane Curvature
P6	Davoudi, Nedasadat	Characterization of Mesenchymal Stem Cells and Microcarriers
P7	Dhara, Madhurima	v-SNARE-based protein-lipid interactions catalyze membrane fusion
P8	Dudek, Johanna	Comprehensive measurements of salivary pellicle thickness formed at different intraoral sites on Si wafers and bovine enamel
P9	Ecker, Nicolas	A phase-field approach for studying actin-wave driven cell migration
P10	Eisenbeis, Janina	Using atomic force microscopy and live cell imaging to unravel new functions of the extracellular adherence protein Eap of Staphylococcus aureus
P11	Faidt, Thomas	Fluoridation of hydroxyapatite - Time dependence and protective properties
P12	Finkler, Marc	Expression regulation by a methyl-CpG binding domain and the incorporation of non-canonical amino acids in an E. coli based, cell-free TX-TL system
P13	Fleury, Jean-Babtiste	New Strategy to Study a Single SNARE Mediated Membrane Fusion Event
P14	Flormann, Daniel	Actin cortex dynamics and structure upon myosin II inhibition
P15	Fredrich, Thierry	Vascular Adaption Dynamics - An old idea probed with modern techniques

P16	Fries, Peter	Influence of actin dynamics on speed and persistence of immune cells
P17	Griffo, Alessandra	Adhesion of cellulose binding modules – a single molecule study
P18	Hadjivasiliou, Zena	Feedback, trafficking and morphogen scaling
P19	Hähl, Hendrik	Lipid-free, pure-protein bilayers and vesicles from native fungal hydrophobins
P20	Hornak, Ivan	Modeling of T-Cell polarization
P21	Jiang, Qiyang	Optoregulation of 3D cellular microenvironments
P22	Jose, Robin	Trapping in and escape time from tree-like structures of neuronal dendrites
P23	Joseph, Desna	A biomaterials platform to Decouple Cell-Matrix and Cell-Cell Forces
P24	Jung, Philipp	Initial adhesion of biofilm forming pathogens to central venous catheters: the role of blood serum proteins
P25	Kale, Sohan	Vertex modeling of epithelial domes and tissue superelasticity
P26	Kaub, Kevin	Development of microtentacles in suspended cells upon inhibition of myosin
P27	Keller, Fabian	Monte Carlo lattice modelling of a bilayer system
P28	Khan, Essak	Photoactivatable Hsp47: An optogenetic tool to regulate collagen assembly & tumor microenvironment
P29	Kirsch, Sonja	P(3,5)P2 lipid binding-induced activation of the human two-pore channel 2
P30	Lemke, Lilia	Proteomic analysis of in-situ initial biofilm
P31	Li, Bin	Interpenetrating Polymer Network Hydrogels with Multiple Local Stiffnesses
P32	Li, Menglin	Space-Time Controlled DNA Cargo Delivery Performed by Active Janus Droplets

P33	Maikranz, Erik	Probabilistic analysis of apoptosis and necrosis in cancer cells induced by natural killer cells
P34	Misch, Johannes Nolle, Friederike	Bacterial adhesion on nanostructured surfaces
P35	Mohammadi-Kambs, Mina	Towards employing fluorescence anisotropy to measure the binding constant of hybridizing oligonucleotide DNA strands
P36	Monzon, Gina	Theoretical modeling of kinesin and dynein gliding assays
P37	Nazarieh, Maryam	Topology preservation of disease-specific gene-regulatory subnetworks
P38	Olsen, Lars Folke	Regulation of glycolytic oscillations by the dynamics of intracellular water
P39	Oriola, David	Spindle pole focusing is controlled by a buckling instability
P40	Peckys, Diana B.	Visualizing single subunits of ORAI channels with STEM to study stoichiometry dependence on activation status
P41	Ramesh, Girish	Calcium-Redox feedback loop in immune cells: New players and regulatory mechanisms
P42	Reda, Bashar	Determination of chlorhexidine by MALDI-TOF MS after application of different chlorhexidine formulations
P43	Renping, Zhao	rofilin 1 reduces CTL migration and survival under high tension
P44	Sadjadi, Zeinab	Modelling the motility of Cytotoxic T Lymphocytes inside infected lymph nodes
P45	Schmidt, Barbara	Reaction-diffusion model for Orai1-STIM1 interaction during CRAC channel formation
P46	Schoppmeyer, Rouven	Human profilin 1 is a negative regulator of CTL mediated cell-killing and migration
P47	Shaebani, Reza	Record Statistics of Non-Markovian Random Walks
P48	Soni, Bhavesh	Intracellular Calcium dynamics during T cell polarization and activation

P49	Spengler, Christian	Enhanced adhesion of Streptococcus mutans to hydroxyappatite after exposure to saliva
P50	Spengler, Christian	Nano-scaled contact area of Staphylococcal cells
P51	Stankevicins , Luiza	The role of vimentin in leukocyte amoeboid migration
P52	Tahan, Nadin	Effect of Different Mouthrinses on Salivary Bacteria in Vivo
P53	Terriac, Emmanuel	Cell cortex structure and dynamics before, during and after adhesion
P54	Vakkeel, Roshna	Poster - Photoactivatable Actin Inhibitor Cytochalasin D
P55	Wettmann, Lukas	Pattern formation of Min proteins in cellular and open geometries
P56	Will, Thorsten	Detecting regulatory protein complexes that define pluripotency
P57	Yamamoto, Akihisa	Cancer Progression Alters Morphological Fluctuation and Migration of Human Gastric Cells
P58	Yazdani, Nazife	Evaluating the protective properties of plant extracts by analyzing the in-situ initial biofilm
P59	Zhang, Jingnan	A platform to study the role of forces in T lymphocyte activation
P60	Zhang, Xin	The role of TMX oxidoreductases in melanoma growth and invasion
P61	Zheng, Yijun	Light-driven force application on individual cell-ECM contacts
P62	Akhmanova, Maria	Modeling of auxin membrane transport and accumulation: implication for study of root growth inhibition by auxin
P63	Salmerón, Jonathan	Spontaneous contraction of poroelastic actomyosin sheets

Abstracts of Invited Talks

I.1 Sub- and supra-cellular mechanisms of tension buffering

Marino Arroyo

Universitat Politècnica de Catalunya-BarcelonaTech, Spain

At the sub-cellular level, cells can buffer membrane tension by the assembly and disassembly of reservoirs [1]. At the tissue scale, recent measurements show that freestanding epithelial monolayers can withstand stretches of about 300% at nearly constant tension [2]. In this talk, I will discuss the sub- and supracellular mechanisms of tension buffering. Interestingly, despite the scale, structural, and molecular differences, there are conceptual commonalities in the way the plasma membrane and cell monolayers control their mechanical state.

[1] Sinha *et al.*, Cell, **144**, 402–413 (2011).

[2] E. Latorre, L. Casares, S.S. Kale, M. Gomez-Gonzalez, M. Uroz, L. Valon, M. Arroyo, X, Trepat, in preparation.

I.2 Porosity Governs Mechanical Properties of Biopolymer Gels

Daniel Bonn[1], Henri C. G. de Cagny[1], Bart E. Vos[2], Mahsa Vahabi[3], Nicholas A. Kurniawan[2], Masao Doi[4], Gijsje H. Koenderink[2], F. C. MacKintosh[3]

[1]Institute of Physics, University of Amsterdam, Science Park 904, 1098 XH Amsterdam, The Netherlands
[2]FOM-Institute AMOLF, Science Park 104, 1098 XG Amsterdam, The Netherlands
[3]Department of Physics and Astronomy, VU, De Boelelaan 1081, 1081 HV Amsterdam, The Netherlands
[4]Center of Soft Matter Physics and its Applications, Beihang University, 100191 Beijing, China

When sheared, most elastic solids including metals, rubbers, and polymer gels dilate perpendicularly to the shear plane. This behavior, known as the Poynting effect, is characterized by a positive normal stress. Surprisingly, fibrous biopolymer gels exhibit a negative normal stress under shear. Here we show that this anomalous behavior originates from the open-network structure of biopolymer gels. Using fibrin networks with a controllable pore size as a model system, we show that the normal-stress response to an applied shear is positive at short times, but decreases to negative values with a characteristic time scale set by pore size. Using a two-fluid model, we develop a quantitative theory that unifies the opposite behaviors encountered in synthetic and biopolymer gels. [1]

[1] H.C. de Gagny *et al.* Phys. Rev. Lett. **117**, 217802 (2016)

I.3 Integrins in synaptic excitability: relevance for neurodevelopmental disorders

Lorenzo A. Cingolani

Center for Synaptic Neuroscience (NSYN), Italian Institute of Technology (IIT), Genova, Italy

Integrins are cell adhesion receptors that serve as physical and functional link between the extracellular matrix and the intracellular cytoskeleton. They are expressed in nearly every cell type, and regulate diverse functions including migration, attachment and differentiation. In the brain, some integrins are enriched at synapses where they regulate synaptogenesis, synapse and dendrite maintenance, and synaptic plasticity. Further, some integrins have been implicated in diverse brain disorders from epilepsy to autism spectrum disorders [1, 2]. Although the physiological role of many integrins in the brain has been extensively studied, it is still unclear how dysfunctions in integrin-mediated cell adhesion alter structural and functional plasticity of dendritic spines, and behavior in mice. To elucidate the molecular and cellular mechanisms linking integrins to synaptic function, we performed morphological, protein chemistry, electrophysiological and behavioral experiments in mice deficient for the synaptic integrin αVβ3. Our results indicate that loss of integrin αVβ3 in neurons does not affect overall brain architecture and the dendritic arborization of neurons, but compromises selectively synaptic transmission, leading to behavioral abnormalities. Our findings support a model whereby integrin αVβ3 is necessary for the correct functioning of excitatory synapses.

[1] M. E. Kerrisk, L. A. Cingolani, and A. J. Koleske, Prog Brain Res 214 (2014) 101.
[2] A. Thalhammer and L. A. Cingolani, Neuropharmacology 78 (2014) 23.

I.4 Force nanoscopy in microbiology

Yves F. Dufrêne

Institute of Life Sciences, Université catholique de Louvain, Croix du Sud, 4-5, bte L7.07.06., B-1348 Louvain-la-Neuve, Belgium

Microbial cells have developed sophisticated multicomponent structures and machineries to govern basic cellular processes, such as chromosome segregation, gene expression, cell division, mechanosensing, cell adhesion and biofilm formation. Because of the small cell sizes, subcellular structures have long been difficult to visualize using diffraction-limited light microscopy. During the last three decades, optical and force nanoscopy techniques have been developed to probe intracellular and extracellular structures with unprecedented resolution, enabling researchers to study their organization, dynamics and interactions in individual cells, at the single molecule level, from the inside out, and all the way up to cell-cell interactions in microbial communities. In this talk, I will discuss the principles of force nanoscopy techniques available in microbiology, and highlight some outstanding questions that these new tools have made possible to answer [1, 2].

[1] Dufrêne YF. Nat Rev Microbiol. 2004, **6**, 451.
[2] Xiao J, Dufrêne YF. Nat. Microbiol. 2016, **1**, 16186.

I.5 Modulation of human ORAI1 channels: modeling and simulations

Rudi Ettrich

Center for Nanobiology and Structural Biology, Institute of Microbiology, Academy of Sciences of the Czech Republic, Zamek 136, CZ-373 33, Nove Hrady, Czech Republic

Orai1 is a calcium-selective channel located in the plasma membrane, and belongs to the family of calcium release activated channels (CRAC) [1]. Orai1, as component of store-operated calcium entry (SOCE), is activated by the second component of SOCE, STIM1, when intracellular calcium stores are depleted. STIM1, located at the endoplasmatic reticulum (ER), senses levels of calcium in the ER and is activated by calcium store depletion. In turn, calcium influx via Orai1 channel refills calcium levels in the endoplasmic reticulum [2]. *Based on the Drosophila melanogaster Orai crystal structure [3] a homology model of human Orai1was prepared that includes extracellular and intracellular loops existing only in the human isoform [4]. The sequence and architecture of Orai channels is unique among other ion channels and suggests a novel gating mechanism. The selectivity filter is formed by a ring of six glutamate residues followed by a hydrophobic and consequent basic region further down the pore. The pore extends into cytosol by approximately 20 Å. Using combined experimental and theoretical approaches this study focuses on the central ion pore to investigate the gating mechanism of this unique channel including altered gating of* Orai1 mutants occurring in tumor cells [6].

[1] M. G. Matias *et al.* "Animal Ca2+ release-Activated Ca2+ (CRAC) Channels Appear to Be Homologous to and Derived from the Ubiquitous Cation Diffusion Facilitators" BMC Research Notes **2010**, 3, 158
[2] S. Feske "CRAC channelopathies" Pflugers Archiv : European journal of physiology **2010**, 460 (2),417-435
[3] X. Hou *et al.* "Crystal Structure of the Calcium Release-Activated Calcium Channel Orai" Science **2012**, 3389 (6112), 1308–1313
[4] I. Frischauf *et al.* "A calcium-accumulating region, CAR, in the channel Orai1 enhances Ca(2+) permeation and SOCE-induced gene transcription" Science Signaling **2015**, 8, ra131
[5] S. Feske *et al.* "A mutation in Orai1 causes immune deficiency by abrogating CRAC channel function" Nature 2006, 441, 179-185

[6] Frischauf *et al.*"Transmembrane helix connectivity in Orai1 controls two gates for calcium dependent transcription", Science Signaling submitted 6/2017, under revision.

I.6 Forces and cytoskeletal dynamics during collective invasion of tumor spheroids

Ben Fabry and Christoph W. Mark

Department of Physics, University of Erlangen-Nuremberg, Erlangen, Germany

Cell movements and associated cell-generated forces are of central importance in cancer metastasis where tumor cells leave a primary tumor and invade the surrounding tissue. This invasion process is driven by cells at the tumor boundary that collectively exert physical forces on the extracellular matrix. To study the physical forces arising from these collective effects, we embed invasive HT-1080 fibrosarcoma spheroids and non-invasive MCF-7 breast carcinoma spheroids in reconstituted collagen matrices. We measure the ongoing deformation of the collagen matrix over time by tracking embedded silica beads in the equatorial plane of the spheroids. We then compute the collective contractile forces from the matrix deformations with a non-linear finite element model. Invasive spheroids reach their maximal contractility after 30 min. Subsequently, overall contractile forces remain constant while cells at the spheroid border invade the matrix. Surprisingly, non-invasive spheroids also generate substantial contractile forces, but these forces rise slowly over the course of 12 hours, and no cells leave the spheroid. We conclude that overall contractility is a poor indicator for cell invasiveness, in contrast to dynamical changes of forces and cytoskeletal reorganization.

I.7 Linking mechanochemistry with protein folding with single bond resolution

Amy E.M. Beedle[1], Marc Mora[1], Steven Lynham[2], Guillaume Stirnemann[3] and Sergi Garcia-Manyes[1]

[1]Department of Physics and Randall Division of Cell and Molecular Biophysics, King's College London, WC2R 2LS, London, UK
[2]Centre of Excellence for Mass Spectrometry, King's College London, SE5 8AF, London, UK
[3]CNRS Laboratoire de Biochimie Théorique, Institut de Biologie Physico-Chimique, Univ. Paris Denis Diderot, Sorbonne Paris Cité, PSL Research University, 13 rue Pierre et Marie Curie, 75005, Paris, France

The nanomechanical properties of elastomeric proteins determine the elasticity of a variety of tissues. Post-translational modifications (PTMs) have recently emerged as a useful tactic to regulate protein nanomechanics. In particular, the presence of covalent disulfide bonds, arguably the most relevant PTM with a significant mechanical role, is a widespread natural strategy to regulate protein extensibility and enhance protein stiffness. The prevalent in-vivo strategy to form disulfide bonds requires the presence of dedicated enzymes. Here we propose two alternative chemical routes to promote non-enzymatic oxidative protein folding through the reactivity of protein based chemical modifications. Using single-molecule force-clamp spectroscopy and mass spectrometry, we first captured the reactivity of an individual sulfenic acid, a PTM that functions as a key sensor of oxidative stress, when embedded within the core of a single Ig domain of the titin protein. Our results demonstrated that sulfenic acid is a crucial short-lived intermediate that dictates the protein's fate in a conformation-dependent manner. When exposed to the solution, sulfenic acid rapidly undergoes further chemical modification, leading to irreversible protein misfolding; when cryptic in the protein's microenvironment, it readily condenses with a neighbouring thiol to create a protective disulfide bond, which assists the functional folding of the protein. A second, alternative method to induce disulfide reformation occurs via disulfide isomerization of naturally occurring small thiols. Our single molecule approach, complemented with DFT calculations revealed that subtle changes in the chemical structure of a transient mixed-disulfide intermediate adduct between a protein cysteine and an attacking low molecular-weight thiol have a dramatic effect on the protein's mechanical stability. Combined, these chemistry-based mechanisms for non-enzymatic oxidative folding provide a plausible

explanation for redox-modulated stiffness of proteins that are physiologically exposed to mechanical forces, such as cardiac titin.

I.8 Environmental stiffness regulates intracellular Ca2+ signals through the proton-sensing receptor

Maike Glitsch

Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, UK

Extracellular acidification and changes in tissue stiffness accompany a range of different diseases including solid cancers and are sensed by cells through activation of cell surface proton-sensing and mechanosensitive receptors, respectively [1, 2].
We find that activation of a particular proton-sensing receptor critically depends on the stiffness of the substrate that cells expressing the receptor are exposed to. The stiffer the substrate, the more reliably and profoundly can the receptor be activated by increases in extracellular proton concentration. Moreover, modulation of proton-sensing receptor activation is a dynamic process; acute changes in substrate stiffness affect proton-sensing receptor activity on a minute time scale. Our results suggest that substrate stiffness-dependent changes in cell shape play a pivotal role in the ability of the proton-sensing receptor to respond to substrate stiffness. Since the activity of the proton-sensing receptor depends on both substrate stiffness and extracellular proton concentration, it acts as a coincidence detector of these two parameters.
Activation of the proton-sensing receptors leads to complex intracellular Ca^{2+} signals that can link to gene transcription [3]. We would like to propose that the coincidence detector of tissue acidification and changes in tissue stiffness is a key player in the progression of certain diseases.

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I.9 Actin as an intranuclear force generator?

Robert Grosse

Biochemisch-Pharmakologisches Centrum Marburg, Philipps-University Marburg, Germany

Nuclear reassembly after mitosis encompasses decondensation of mitotic chromosomes and is integral for establishing functional nuclear architecture. Live imaging as well as atomic force microscopy of mitotic mammalian cell nuclei revealed nuclear protrusions driven by transient assembly of actin filaments. Nuclear F-actin assembled during early G1 phase and is dynamically reorganized to facilitate nuclear volume expansion. Compartment-specific inhibition of nuclear F-actin assembly significantly impaired nuclear protrusions, volume expansion as well as chromatin decondensation, characterised by altered histone modifications, a higher degree of chromatin compaction as well as an increased proportion of heterochromatin. Failed chromatin decondensation due to a loss of nuclear F-actin after mitosis leads to decreased gene expression and proliferation upon cell cycle progression. Phalloidin-based mass-spec studies at mitotic exit identified the actin-disassembling factor Cofilin-1 as a nuclear F-actin-binding protein. Optogenetic analysis revealed a critical function of Cofilin-1 in regulating nuclear actin dynamics and volume expansion after mitosis.

I.10 Biophysical techniques for the study of phase transitions in cells

Raimund Schlüßler[1], Shada Abu Hattum[1], Mirjam Schürmann[1], Paul Müller[1], Gheorghe Cojoc[1], Felix Reichel[1], Kyoohyun Kim[1], Jürgen Czarske[2], Simon Alberti[3], and Jochen Guck[1]

[1]Biotechnology Center, Technische Universität Dresden, Germany
[2]Laboratory of Measurement and Sensor System Techniques, Technische Universität Dresden, Germany
[3]Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

Recently, phase transitions of protein-RNA droplets in cells, and of the cytoplasm of entire cells [1], have been shown to play important roles in physiological and pathological processes in biology. Their molecular control is still unclear at this point. We have applying a range of biophysical techniques for the specific study and quantitative characterization of such phase transitions. We use a dual-beam laser trap, real-time deformability cytometry and atomic force microscopy for the viscoelastic characterization of cells and protein-RNA granules in vitro. We combine opto-fluidic object rotation with quantitative phase microscopy to obtain phase images from multiple angles, which in turn are tomographically reconstructed by a back-propagation algorithm [2] to obtain 3D distributions of refractive index and mass density inside trapped objects [3]. Finally, we have also established Brillouin microscopy for the 3D mapping of mechanical properties inside cells with diffraction-limited resolution. I will present and discuss our findings obtained with this unique toolset.

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I.11 Action at a Distance in the Yeast Nucleus

Jane Kondev

Physics Department, Brandeis University, Waltham (MA), USA

Various functions performed by chromosomes, such as transcription regulation and DNA recombination involve long-range communication between DNA sequences that are hundreds of thousands of bases apart along the chromatin, and microns apart in the nucleus. I will discuss two modes of long-range communication in the nucleus, chromosome looping, which brings distant DNA sequences in close spatial proximity, and protein-sliding between distant sequences along the chromosome, both in the context of DNA-break repair in yeast.

Yeast is an excellent model system for studies that link chromosome shape to its function as there is ample experimental evidence that yeast chromosome conformations are described by a simple polymer model. Using a combination of polymer theory and cell experiments, I will show that loss of polymer entropy due to chromosome looping serves as the driving force for homology search during repair of broken DNA. I will also discuss the spread of histone modifications away from the DNA break point in the context of simple physics models based on chromosome looping and protein sliding, and show how combining physics theory and cell-biology experiment can be used to dissect the molecular mechanism of the spreading process. The key goal is to show how combined theoretical and experimental studies reveal physical principles of long-range communication in the nucleus.

I.12 Cytoskeletal Intermediate Filaments – from Self-Assembly to Cell Mechanics

Sarah Köster

Institute for X-Ray Physics, University of Göttingen, Göttingen, Germany

The cytoskeleton consists of three filamentous systems, actin filaments, microtubules and intermediate filaments (IFs) and has been identified as a main player in cell mechanics. Among the three filamentous systems, IFs self-assemble in a highly hierarchical process giving rise to a very particular molecular architecture. IFs are expressed in a cell type specific manner and are thus being discussed as strong candidates for the precise definition of the different mechanical properties of different cell types. Our research focuses on the relation between molecular structure and mechanical properties of filaments and cells. I will present state-of-the art experiments and recent results on the self-assembly of the proteins into filaments and networks and their intriguing mechanical properties. The relevant length scales for these processes range between few nanometers and many micrometers. Therefore, we employ small angle x-ray scattering (SAXS), x-ray nano-diffraction, static and dynamic light scattering (SLS/DLS), fluorescence correlation spectroscopy (FCS), optical tweezers, and fluorescence microscopy. As some of these methods are inherently slow and thus provide only a low time resolution, we combine the observation techniques with microfluidics to obtain in situ data.

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I.13 Tackling cell deformation, division and migration by a combination of experiments and computational models

Caterina A. M. La Porta[1] and Stefano Zapperi[2]

[1]Center for Complexity and Biosystems, Department of Environmental Science and Policy, University of Milan, Milano, Italy, and
[2]Center for Complexity and Biosystems, Department of Physics, University of Milan, Milano, Italy

In this talk, we review our recent results related to the observation and modeling of cell deformation, division and migration [1]. We first discuss our experiments demonstrating that water transport in and out of the cell is needed for the formation of blebs, commonly observed protrusions in the plasma membrane driven by cortex contraction. Simulations of a model of fluid-mediated membrane-cortex deformations show that a permeable membrane is necessary for bleb formation which is otherwise impaired [2]. Next, we discuss two mechanical models for individual and multiple cell divisions: i) A three dimensional model of motor-driven chromosome congression and bi-orientation during mitosis revealing that successful cell division requires control of the total number of microtubules [3]. ii) A model for the division of stem cells in a crypt that relates stem cell population dynamics to the effect of mechanical forces acting on the spindle. We observe that the mechanically induced strategy for development is sub-optimal and crucially depends on the stiffness of the spindle [4]. Finally, we discuss the observation of universal activity bursts in collective cell migration [5].

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I.14 Phase Transitions, Non-equilibrium Fluctuations and Broken Detailed Balance in Biological Systems

Frederick MacKintosh

Departments of Chemical & Biomolecular Engineering, Chemistry and Physics & Astronomy and Center for Theoretical Biological Physics, Rice University Houston, Texas, USA

Living cells are kept far out of equilibrium by metabolic processes and energy-consuming molecular motors that generate forces to drive the machinery behind various cellular processes. Such active processes give rise to both directed motion and stochastic fluctuations in living systems at both intracellular and extracellular scales. We describe recent advances both in theoretical modeling of such activity, as well as experiments on reconstituted *in vitro* acto-myosin networks and living cells. We show how internal force generation in cellular networks can both control network stability and give rise to diffusive-like motion. We show that active stresses in model networks can also lead to a novel percolation-like transition that exhibits features of both first- and second-order phase transitions. As a result of enzymatic activity at the molecular scale, living systems characteristically violate *detailed balance*, a fundamental principle of equilibrium statistical mechanics. We show how this leads to violations of detailed balance at the meso-scale in living systems.

I.15 Correlating bacterial interaction forces with biofilm structure

Berenike Maier

Physics Department, University of Cologne, Germany

Communities of bacterial cells can live together embedded within a slime-like molecular matrix as a biofilm. This allows the bacteria to hide from external stresses. A single bacterium can replicate itself and develop into a biofilm, and over time the bacterial cells in specific regions of the biofilm will start to interact with their neighbors in different ways. These interactions occur via structures on the surface of the bacterial cells, and the differences in these interactions resemble those that occur as cells specialize during the development of animal embryos. Previous research into embryonic development has shown how differences in the physical interactions between embryonic cells are essential for sorting the cells into their correct locations and shaping the embryo. Recently, we found that the basic physical principles are similar in bacterial biofilms.

In my talk I will discuss how mechanical interactions between bacteria govern the structure and dynamics of bacterial biofilms. We have generated a molecular toolbox that allows tuning the interaction forces systematically. Using this toolbox, we address the question how differential interaction forces govern cell sorting and biofilm structures in general. Currently, we are evaluating how biofilms might benefit from the structures that develop due to differential interactions.

I.16 Cytoskeletal Mechanics of Blood Platelets

Aastha Mathur, Serge Dmitrieff, Sandra Correia, Romain Gibeaux, Iana Kalinina, Tooba Quidwai, Jonas Ries and Francois Nedelec

Cell Biology and Biophysics, EMBL Heidelberg, Germany

The cytoskeleton is a conserved filamentous system made of proteins that are specialized into scaffolding and force production in living cells. It drives many essential processes *in vivo.*
Such as cell division, cell motility and morphological changes. The cytoskeleton is a dynamic and versatile system that can adopt different architectures, depending on the task at hand. A general objective of our research is to analyze the dynamics and mechanical properties of these architectures to understand how they are adapted to perform their particular role. In this talk, I will first introduce the physical characteristics of the cytoskeletal components, and the different approaches that are used to study the collective behavior of cytoskeletal systems. I will then present with our experimental characterization of blood platelets, which play a major role in hemostatis, the process of stopping blood loss from injured vessels. While floating free in the blood in the so called 'resting' state, platelets have a discoid shape. Their size in this case can be understood from the competition between the elasticity of a circular bundle of microtubules, and surface tension at the cell edge. Such a mechanical equilibrium predicts a scaling law that is verified by imaging a large number of individual platelets live, from Mouse and Human blood samples. I will then discuss the dynamics that is observed at the onset of platelet activation, on the path towards platelet adhesion and aggregation. The ring maintaining the shape of platelets initially coils, but is able to recover within 30 minutes. This can be explained as the ring is made of microtubules that alternate between growing and shrinking states, and can reform with a smaller radius. Importantly, we find that this response is dependent on the size of platelets, with possible implications for the physiology of platelets *in vivo.*

I.17 A molecular mechanism for Orai1 channel activation by STIM1

Raz Palty

Department of Biochemistry, The Rapaport family faculty of medicine, Technion – Israel Institute of Technology, Haifa, Israel

Store operated calcium entry (SOCE) represents a key mechanism by which cells generate Ca^{2+} signals and maintain Ca^{2+} homeostasis by replacing Ca^{2+} lost from endoplasmic reticulum (ER) with Ca^{2+} that enters the cytoplasm through plasma membrane channels. SOCE was characterized biophysically over a 20-year period and the field exploded recently with the identification of the genes that encode its essential proteins. The primary components are STIM1, the Ca^{2+} sensor of the ER, which is activated when the ER is depleted of Ca^{2+} and then activates the plasma membrane Ca^{2+}release activated Ca^{2+} (CRAC) channel, and Orai1, the CRAC channel pore forming subunit. Abnormal SOCE due to aberrant expression or function of STIM1 and Orai1 is implicated as a leading cause of several diseases including chronic inflammation, muscle weakness, and a severe combined immunodeficiency syndrome. Yet, although the process of Orai1 channel activation by STIM1 has been intensely investigated the molecular and structural basis of how STIM1 regulates the opening of the Orai1 channel pore remains poorly understood. Here, I will discuss recent work in our laboratory that seeks to understand how coupling with STIM1 leads to molecular rearrangements in the Orai1 channel protein underlying the opening of the channels pore.

I.18 Physical and biological aging of red blood cells

Marta Gironella[1] and Felix Ritort[1,2]

[1]*Physics School, Condensed Matter Physics Department, University of Barcelona, C/Marti i Franques s/n, 08028 Barcelona, Spain*
[2]*Ciber-BBN Center for Bioengineering, Biomaterials and Nanomedicine, Instituto de Salud Carlos III, Madrid, Spain*

Red blood cells (RBC) are probably the most simple and abundant kind of cells inmammals. Mature RBC are not considered living cells but sacks mostly containinghemoglobin that are surrounded by a plasma membrane containing the inner layer cell cortex, a meshwork of spectrin and others fibrous proteins that determines its mechanical properties. The main metabolic activity of RBC is the steady ATPproduction from glucose along the glycolysis pathway, apparently leading to anonequilibrium steady-state state which, however, slowly ages (*in-vivo* and *in-vitro*) due to accumulated alterations such as oxidative stress, osmotic imbalance, membrane vesiculation and shrinkage, etc.. Here we have investigated the time-dependent mechanical response of red blood cells by deforming the plasma membrane in *in-vitro* optical tweezers assays. We have determined the characteristic relaxational timescales for RBC shape recovery in a series of experimental protocols such as force-jump and repeated stretching-releasing cycles. We report on memory and physical aging effects in the experiments and discuss the relation between such effects and biological aging.

I.19 Force triggers YAP nuclear entry by mechanically regulating transport across nuclear pores

Alberto Elosegui-Artola[1], Ion Andreu[2,3], Amy Beedle[4,5], Ainhoa Lezamiz[4,5], Marina Uroz[1], Anita Kosmalska[1,6], Roger Oria[1,6], Catherine M. Shanahan[7], Xavier Trepat[1,6,8,9], Daniel Navajas[1,6,10], Sergi Garcia-Manyes[4,5], and Pere Roca-Cusachs[1,6]

[1]*Institute for Bioengineering of Catalonia,Barcelona Ins Barcelona 08028, Spain.*
[2]*Mondragon University, 20500 Arrasate, Spain.*
[3]*CEIT and TECNUN (University of Navarra), 20018 Donostia-San Sebastian, Spain.*
[4]*Randall Division of Cell and Molecular Biophysics, King's College London, London SE1 1UL, UK.*
[5]*Department of Physics, King's College London, London WC2R 2LS, UK.*
[6]*University of Barcelona, 08028 Barcelona, Spain.*
[7]*Cardiovascular Division, James Black Centre, King's College, London SE59NU, UK.*
[8]*Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain.*
[9]*Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina, 28029 Madrid, Spain.*
[10] *Centro de Investigación Biomédica en Red en Enfermedades Respiratorias, 28029 Madrid, Spain.*

YAP is a mechanosensitive transcriptional activator with a critical role in cancer, regeneration, and organ size control. Here we show that force applied to the nucleus directly drives YAP nuclear translocation by decreasing the mechanical restriction of nuclear pores to molecular transport. We demonstrate that the nucleus only connects mechanically to the cytoskeleton above a threshold in substrate rigidity, allowing forces exerted through focal adhesions to reach the nucleus. This leads to nuclear flattening, which increases YAP nuclear import by decreasing the mechanical restriction of nuclear pores to molecular transport. This restriction is further regulated by the mechanical stability of the transported protein. Control of YAP translocation by nuclear force is independent of focal adhesions, the actin cytoskeleton, substrate rigidity, cell-cell adhesion, and the Hippo pathway. Our results unveil a mechanosensing mechanism mediated directly by nuclear pores, demonstrated for YAP but with potential general applicability in transcriptional regulation.

I.20 Emergence of elasticity in adherent cells

Ulrich S. Schwarz

Institute for Theoretical Physics and BioQuant, Heidelberg University, Heidelberg, Germany

All adherent cell types actively exert forces to their substrates, as demonstrated by traction force microscopy [1]. On the molecular scale, forces are generated and propagated by supramolecular complexes with typical turnover times of seconds. On larger length scales, these molecular processes are expected to lead to viscoelastic behaviour, as observed for e.g. lamellipodia or the actin cortex. In the context of mature adhesion, however, cells build systems of contractile bundles that can maintain high forces in a seemingly static and elastic manner [2]. Experimentally, the mechanics and stabiliy of these systems can be challenged by e.g. laser cutting [3] or optogenetic activation of contractiliy [4]. In both cases, data analysis based on mathematical models provides strong evidence for an effectively elastic behaviour of cell mechanics. Strikingly, this elastic behaviour can be switched to viscoelastic behaviour by blocking the repair protein zyxin [4], suggesting that continuous repair is required to keep the system effectively elastic. The importance of elastic effects can also be demonstrated in a non-invasive manner by analyzing cell shape in 3D-scaffolds with a mathematical model [5]. This suggests that cells use elastic effects to generate higher forces than would be possible by contractility alone.

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I.21 Optimal decoding of cellular identities in a genetic network

Gasper Tkaĉik[1], Mariela D. Petkova[2], William Bialek[2], Eric F. Wieschaus[2] and Thomas Gregor[2]

[1]*IST Austria, Klosterneuburg, Austria*
[2]*Princeton University, Princeton, New Jersey, USA*

In developing organisms expression levels of multiple patterning genes determine spatially prescribed cell identities. It is unclear, however, what rules govern this specification, what is its precision, and how early in development it occurs. Using the gap gene network in the early fly embryo as an example, we show how expression levels of the four gap genes can be combined—or jointly decoded—into an optimal specification of position, which is precise to 1% of the embryo's length. As a test we apply this decoder to distorted patterns of gap gene expression in embryos lacking various primary maternal inputs. Output of the gap gene network are pair-rule genes producing each seven stripes along the embryo. We show that the decoder correctly predicts, with no free parameters and 1% accuracy, the patterns of these pair-rule stripes also in mutant backgrounds. Our results imply that individual cells use developmental enhancers to implement a mathematically optimal decoding strategy, in which developmental precision emerges from a simultaneous and absolute readout of all four gap gene levels. Precise cell identities are thus available at the earliest stages of development, in contrast to the prevailing view that positional information must be refined slowly across successive layers of the patterning network.

I.22 Physical forces driving migration, division and folding of epithelial sheets

Xavier Trepat

ICREA @ Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

Biological processes such as morphogenesis, tissue regeneration, and cancer invasion are driven by collective migration, division, and folding of epithelial tissues. Each of these functions is tightly regulated by mechanochemical networks and ultimately driven by physical forces. I will present maps of cell-cell and cell-extracellular matrix (ECM) forces during cell migration and division in a variety of epithelial models, from the expanding MDCK cluster to the regenerating zebrafish epicardium. Force maps show that cells dividing in a migrating epithelium exert large cell-ECM forces during cytokinesis. These forces point towards the division axis and are exerted through paxillin-rich focal adhesions that connect the cytokinetic ring to the underlying ECM. Large forces at these adhesions are associated with failure of cytokinesis and polyploidy, indicating that abnormal cell-matrix adhesion at the cleavage furrow impedes abscission. Time lapse analysis of force maps further reveals that cell-cell forces determine the duration of the cell cycle and mitosis. Finally, I will present direct measurements of epithelial traction, tension, and luminal pressure in three-dimensional epithelia of controlled size and shape. Strikingly, we found that epithelial tension in the free-standing curved monolayers is constant up to 200% strain, indicating active mechanisms of tensional homeostasis.

I.23 Control of cancer cell invasion by nuclear deformability

Katarina Wolf

Department of Cell Biology, RIMLS, Radboud University Medical Centre, 6500 HB Nijmegen, The Netherlands

Tumor cell migration through 3D tissue depends on a physicochemical balance between tissue constraints, contact-dependent ECM degradation, and deformability of cell and nucleus, respectively. With a focus on lamin- and chromatin-mediated mechanics of the cell nucleus, I will dissect the relative contributions of these parameters under conditions of space confinement in substrate geometries that mimick connective tissue structures *in vivo.*

I.24 Egulation of actomyosin contractility: lessons from C. *elegans*

Ronen Zaidel-Bar

Department of Cell and developmental biology, Faculty of medicine, Tel-Aviv University, Tel-Aviv, Israel

Distinct actomyosin structures power a variety of cellular and multicellular processes requiring force. A network of proteins, including actin binding proteins, myosin phosphorylation regulators, and RhoGTPases and their regulators (collectively referred to as the Contractome), regulates the assembly and contraction of actomyosin structures in specific cellular locations at specific times. How this regulation works in vivo is still poorly understood. We are addressing this question in the model organism C. elegans. In my talk, I will present recent results on the function of contractility in maintaining the structure of the syncytial germline, a mechanotransduction pathway linking membrane stretching to activation of actomyosin in the spermatheca, the role of connectivity in cortical polarization and cytokinesis in the zygote, and an unexpected role for non-junctional cadherin clusters.

Abstracts of Contributed Talks

C.1 Modeling of epithelial sheet deformation under external force applied by a migrating cell

Maria Akhmanova, Aparna Ratheesh, Daria E. Siekhaus

IST Austria, Klosterneuburg, Austria

Mechanics of living cells and tissues play a central role in many phenomena, from morphogenesis to cell migration [1][2]. One prominent example is the epithelia – a sheet of cells tightly attached to one another[3]. In the Drosophila embryo, immune cells migrate along the inner (basal) side of an epithelial layer during their invasion into the germband [4] and during this process exert a force on the epithelial sheet that deforms it. The mechanical properties of epithelial cells, in particular, surface tension and stiffness influence deformability of the sheet and, thus, the speed of migrating cells. Computational models can help to dissect how the tissue mechanics emerges from mechanical properties of individual cells.

We constructed a finite-element model of an epithelial sheet using COMSOL Multiphysics software. The cell cortex, modeled as an elastic shell, is divided into 3 domains with distinct properties (apical, lateral and basal)[3]. Force exerted by a migrating cell is applied to examine apparent stress-strain behavior of the sheet. Our model shows that similar shifts in tension of the different cortex domains distinctly affect sheet deformability, with the highest contribution from the basal domain. This study contributes to understanding how a mutual mechanical balance is achieved in tissues to allow for robust mechanical events, such as cell translocation[5].

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C.2 Bleb nucleation through membrane peeling

Ricard Alert and Jaume Casademunt

Departament de Física de la Matèria Condensada, Universitat de Barcelona, Barcelona, Spain

Blebs are cellular protrusions arising from a local detachment of the cell membrane from the underlying actomyosin cortex. We study the nucleation of blebs by means of a simple model in which membrane-cortex adhesion is mediated by elastic linker proteins with force-dependent binding kinetics [1]. The model shows that bleb nucleation is governed by membrane peeling, namely the fracture propagation process whereby adjacent linkers sequentially unbind. By this mechanism, the growth or shrinkage of a detached membrane patch is completely determined by the linker kinetics, regardless of the energetic cost of the local detachment. We predict the critical nucleation radius for membrane peeling and the corresponding effective energy barrier. These are typically smaller than those predicted by classical nucleation theory, implying a much faster nucleation. We also perform simulations of a continuum stochastic model of membrane-cortex adhesion to obtain the statistics of bleb nucleation times as a function of the pressure on the membrane. The determinant role of membrane peeling changes our understanding of bleb nucleation, opening new directions in the study of blebs.

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C.3 Hydrodynamic instabilities, waves and turbulence in spreading epithelia

C. Blanch-Mercader[1] and J. Casademunt[2]

[1]Department of Biochemistry, Faculty of Sciences, University of Geneva, Geneva, Switzerland, and
[2]Department d'Estructura i Constituents de la Matèria, Facultat de Química i Física, Universitat de Barcelona, Barcelona, Spain.

In recent years a great deal of attention has been focused on the modelling and understanding of freely expanding epithelial monolayers, as a model system to study morphogenesis, tissue repairing or cancer invasion. These cellular systems exhibit a rich repertoire of dynamical behaviours. In particular, some puzzling observations have revealed the existence of elastic waves at time scales of several hours where one would expect a fluid-like behaviour [1]. In our study, we show that these observations can be conciliated through a minimal model of a thin active gel by introducing two sources of activity: traction forces with the environment and intercellular contractile stresses. Our physical model harbours a new periodic oscillatory instability controlled by the cell-sbstrate interaction. The anomalous phase of the stress-strain rate oscillations is not universal, unlike Newtonian fluids, but depends on the material properties of tissues. Near criticality, the system admits a reduced description in the terms of the Complex Ginzburg-Landau equation, for which we derived analytically the mapping, providing a complete characterisation of the d ynamical states of the system, which are comprised between coherent nonlinear waves to turbulent states. We compare these results with recent experimental observations [1-3] on these cellular system and bring to light novel predictions.

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C.4 Autocatalytic microtubule nucleation determines the size and mass of spindles.

Franziska Decker, David Oriola, Benjamin Dalton, Jan Brugués

Max Planck Institute of Molecular Cell Biology and Genetics.
Max Planck Institute for the Physics of Complex Systems.
Pfotenhauerstraße 108, 01307, Dresden, Germany

Regulation of size and growth is a fundamental problem in biology. A prominent example is the formation of the mitotic spindle, where protein concentration gradients around chromosomes are thought to regulate spindle growth by controlling microtubule nucleation [1][2]. Previous evidence suggests that microtubules nucleate throughout the spindle structure [3-5]. However, the physical mechanisms underlying microtubule nucleation and its spatial regulation are still unclear. Here, we developed an assay based on laser ablation to directly probe microtubule nucleation events in Xenopus laevis egg extracts. Combining this method with theory and quantitative microscopy, we show that the size of a spindle is controlled by autocatalytic growth of microtubules, driven by microtubule-stimulated microtubule nucleation. The autocatalytic activity of this nucleation system is spatially regulated by the availability of the active form of the small GTPase Ran, which decreases with distance from the chromosomes. Thus, the size of spindles is determined by the distance where one microtubule nucleates on average less than one new microtubule. This mechanism provides an upper limit to spindle size even when resources are not limiting and may have implications for spindle scaling during development.

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C.5 Active wetting of epithelial tissues

R. Alert[1], C. Pérez-González[2], C. Blanch-Mercader[3], X. Trepat[2], J. Casademunt[1]

[1]Departament de Física de la Matèria Condensada, Universitat de Barcelona, Spain
[2]Institute for Bioengineering of Catalonia, Barcelona, Spain
[3]Laboratoire Physico Chimie Curie, Institut Curie, Paris, France

Collective cell migration in freely spreading epithelia in controlled environments has become a landmark in our current understanding of fundamental biophysical processes in development, regeneration, wound healing and cancer. Here we study experimentally and theoretically the mechanics of an epithelial monolayer by extending the classical concept of wetting to an active material that generates contractile stresses and exerts active traction on the substrate. The tissue is modelled as an active polar viscous fluid, and the advance or retraction (wetting vs de-wetting) of the monolayer front is understood as the result of the competition between contractility and traction. The model and the experiments show excellent quantitative agreement in a broad variety of aspects, thus building a complete physical picture of the mechanics of the problem. The emerging scenario introduces novel features with no counterpart in classical wetting phenomena, such as the e xistence of a critical wetting size or the morphological instability of retracting fronts during de-wetting. In all, our results emphasize the collective nature of dynamical modes in spreading epithelia, as a result of the long-range hydrodynamic coupling of the tissue understood as an active polar fluid.

C.6 Organ size control via the interplay between luminal pressure and cell mechanics

Chii Jou Chan[1], Ryan Petrie[2], Takashi Hiiragi[1]

[1]*EMBL Heidelberg, Heidelberg, Germany*
[2]*Drexel University, Pennsylvania, US*

Organ size control is fundamental in animal development. However, the underlying mechanisms acting across the scales from the whole multi-cellular tissues to single cells remain elusive. Given that luminal formation is universal in epithelial tissues, fluid pressure may play a substantial role during morphogenesis [1]. Here, we use early mouse embryos and combine genetics and biophysics to understand the mechanisms by which cell fate specification is coordinated with organ size control. Mammalian embryogenesis involves the formation of a fluid-filled cavity in the blastocyst. We showed that the cortical tension of the cells surrounding the blastocyst cavity is developmentally controlled. This is achieved by multiple feedback loops between the luminal pressure, tissue/cell geometry, cortical tension and cell-cell adhesions operating from sub-cellular to whole organism scales. In contrast with previous models based on cell proliferation and growth, our findings reveal the integral roles of fluid and tissue mechanics in controlling organ size and development.

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C.7 Non-Linear dynamics of beating cardiomyocytes

Ohad Cohen, and Samuel Safran

Department of Materials and Interfaces, Weizmann Institute of Science, Rehovot 76100, ISRAEL

Recent experiment by the group of Tzlil [1] have shown that nearby cardiac cells seeded (49 100 micrometers apart) on an elastic gel, synchronize their beating phase and frequency even without direct contact. By introducing an inert probe that induced periodic elastic deformations in the substrate, the experiments showed that one can pace beating cardiac cells that are relatively far from the probe. The time required to pace the cell was on the order of 49 15 min, and the cell maintained the new beating frequency for as long as 49 1 hr after the probe was removed. These long time scales are in complete contrast to the very short time scales (49 1 sec) that characterize relaxation after electrical stimulation is removed [1].

We predict and compare with experiment [1] the dynamical states and persistence time of a beating cardiomyocyte, using a non-linear oscillator model motivated by acto-myosin dynamical contractility [2, 3]. This model was recently applied to hair cells in the ear, where the eect of varying the amplitude of an oscillating signal (sound wave) on these cells was examined. It was shown that the non-linear mechanical response is crucial in for the excitation of hair bundles due to specic tone frequencies [4, 5, 6].

Our findings relate to the coupled beating of two nearby cells, or a cell paced by a nearby mechanical probe. We begin in Sec. ?? with a simple, analytical treatment of the deterministic dynamics that predicts spontaneous, entrained beating (with the probe frequency) and \bursting" (short periods of entrainment to the probe separated by quiescence) of paced cells, and predict how these depend on the probe amplitude and frequency, in agreement with experiment [1]. We further consider the interesting eects of small noise on the non-linear oscillator model of the beating cell [7], and show how it aects the coherence of beating. Finally, we predict the dependence of time required for a cell to transition from spontaneous to entrained beating once the probe is applied as well as its dependence on the probe amplitude. We account for the origin of the much longer time scale (minutes) required to entrain spontaneously beating cells by considering biological adaptation (which delays the response of the cell to the external signal).

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C.8 Graphene liquid-enclosure facilitates single protein analysis in whole cells by electron microscopy

Indra Navina Dahmke[1], Andreas Verch[1], Diana B. Peckys[2], Robert Weatherup[3], Stephan Hofmann[4], and Niels de Jonge[1,5]

[1]INM Leibniz Institute for New Materials, Saarbrücken, Germany
[2]Department of Biophysics, Saarland University, Homburg, Germany.
[3]Department of Chemistry, University of Cambridge, Cambridge, UK
[4]Department of Engineering, University of Cambridge, Cambridge, UK
[5]Department of Physics, Saarland University, Saarbrücken, Germany

Membrane proteins regulate many important cellular functions via dynamic assembly into active complexes. Yet, analytical methods to study their distribution in the intact plasma membrane are still limited. Therefore, we used a graphene liquid-enclosure to enable high resolution electron microscopy (EM) of single, whole cells for the analysis of membrane protein distribution in the context of the corresponding cellular region.

For this purpose, SKBR3 cells were grown on silicon microchips and stained with quantum dots (QDs) bound to specific peptides to label the ErbB2 growth factor receptor. The samples were covered with graphene films and imaged with correlative light microscopy and EM. Scanning transmission EM (STEM, 200 kV) enabled statistical analyses of the distribution into single, paired and clustered ErbB2 proteins. We compared different membrane structures, such as ruffles or tunneling nanotubes, to flat cellular regions and found increased homodimerization of ErbB2 proteins at these sites.

In conclusion, the graphene liquid-enclosure allowed single-molecule analysis of membrane proteins in intact, hydrated cells.

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C.9 Analysis of ion channel stoichiometry within single cells via liquid-phase electron microscopy and modeling

Diana B. Peckys[1], Dalia Alansary[1], Christof Stoerger[2], Veit Flockerzi[2], Barbara A. Niemeyer[1] and Niels de Jonge[3,4]

[1]*Molecular Biophysics*
[2]*Experimental and Clinical Pharmacology and Toxicology, Saarland University, Homburg/Saar, Germany*
[3]*INM Leibniz Institute for New Materials, and*
[4]*Department of Physics, Saarland University, Saarbrücken, Germany*

The stoichiometry of membrane protein complexes forming ion channels varies between different functional states. Most knowledge about the stoichiometry-function relationship has been obtained from pooling materials from many cells, and using methods such as x-ray crystallography, and gel electrophoresis thus obtaining information about population averages only. We have employed liquid-phase scanning transmission electron microscopy [1] to directly image individual channels within intact cells. Two different channels were studied, ORAI1 proteins forming ion channel subunits of the Calcium Release Activated Calcium channel complex [2], and hTMEM16A forming a calcium-activated chloride channel [3]. Quantum dot nanoparticles were specifically attached to the proteins for their detection. Electron microscopy images revealed the individual label locations. This data was analyzed using the pair correlation function, and an analysis of cluster size and frequency was performed. The experimental results were compared to a mathematical model involving cluster probabilities as function of the labeling efficiency from which it was deduced that ORAI1 was present in hexamers in a small fraction, and mostly in monomers and dimers. hTMEM16A, on the other hand, resided in the plasma membrane as dimer only and was not present as monomer.

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C.10 Rupture dynamics and chromatin loss in deformed nuclei

Dan Deviri

Weizmann institute of science, Rehovot, Israel

During migration of cells in vivo, in both pathological processes such as cancer metastasis or physiological events such as immune cell migration through tissue, the cells must move through narrow interstitial spaces which can be smaller than the nucleus. This can induce deformation of the nucleus which, according to recent experiments, may results in rupture of the nuclear envelope that can lead to cell death, if not prevented or healed within an appropriate time. The nuclear envelope, which can be modeled as a viscoelastic gel whose elasticity and viscosity primarily depend on the lamin composition, may utilize mechanically induced, self-healing mechanisms that allow the hole to be closed after the deformation-induced strains are reduced by leakage of the internal fluid. Here, we present a viscoelastic model of the evolution of holes nucleated by deformations of the nuclear envelope and estimate the loss of chromatin through the rupture and its relation to the lamin A/C to B ratio in the nuclear envelope.

C.11 Mechanical responses of axonal cytoskeleton

Sushil Dubey[1], Jagruti Pattadkal[2], Aurnab Ghose[2], Andrew callan-Jones[3], Pramod Pullarkat[1]

[1]Soft Condensed Matter Group, Raman Research institute, Bangalore, India
[2]Department of biology, Indian Institutes of Science Education and Research, Pune India
[3]Laboratory of Matter and Complex Systems, Paris-Diderot University, Paris, France

The mechanical properties of the axonal cytoskeleton play an important role in development (growth and retraction) [1],[2],[3]. We are studying the mechanical responses of neurons using a home-built Force Apparatus which is an optical fiber based instrument [4]. Mechanical response of neuronal cells subjected to tension using the force apparatus shows a non-linear viscoelastic behavior. We are also studying stress relaxation and creep behavior of the axon. Axons also show a transition from a viscoelastic elongation to active contraction and we aim to investigate the mechanism responsible for this effect [5]. In short we plan to study (a) the roles played by the different cytoskeletal components, including motor proteins and MAPs in regulating the mechanical properties of axons, and (b) in exploring the feedback mechanism that regulate tension induced growth of axons. Our results show that f-actin plays important role in maintaining axonal tension which could be due to spectrin-actin skeleton arranged in periodic fashion [6].

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C.12 What can we learn from the observation of red blood cell membrane flickering?

Herve Turlier[1], Thorsten Auth[2], Basile Audoly[3], Nir Gov[4], Cecile Sykes[5], Jean-Francois Joanny[5], Gerhard Gompper[2], Timo Betz[6], and Dmitry A. Fedosov[2]

[1]*European Molecular Biology Laboratory, Meyerhofstrasse 1, 69117 Heidelberg, Germany*
[2]*Institute of Complex Systems, Forschungszentrum Jülich, 52425, Jülich, Germany*
[3]*CNRS, Institut Jean Le Rond d'Alembert UMR7190, 4 place Jussieu, 75005 Paris, France*
[4]*Department of Chemical Physics, Weizmann Institute of Science, Rehovot, Israel 76100*
[5]*Institut Curie, PSL Research University, CNRS, UMR 168, 75005 Paris, France*
[6]*Institut of Cell Biology, ZMBE, Von-Esmarch-Strasse 56, 48149 Münster, Germany*

Red blood cells are seen to flicker under optical microscopy, a phenomenon initially described as thermal fluctuations of the cell membrane [1]. However, recent studies indicate that the membrane flickering can be shape and position dependent, and can have a contribution from non-equilibrium (active) processes [2,3]. These studies call into question most simple models used for the connection between membrane fluctuations and its mechanical properties, making the interpretation of flickering measurements unreliable. We employ realistic stochastic simulations of red blood cells to investigate the dependence of membrane fluctuations on the position of measurements and to decouple passive (thermal) and active contributions to the observed flickering. Simulations indicate that it should be possible to quantitatively extract red blood cell membrane properties, including shear elasticity, bending rigidity, and membrane viscosity. We also suggest several possibilities for the decoupling of passive and active contributions to the membrane flickering. Finally, we will discuss potential mechanism responsible for the active contribution.

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C.13 Homo- and Heterodimerization of G protein coupled Chemokine receptors

Stefan Gahbauer[1], Kristyna Pluhackova[1], and Rainer A. Böckmann[1]

[1]*Computational Biology, Department of Biology, Friedrich-Alexander University Erlangen-Nürnberg, Erlangen, Germany*

G protein coupled chemokine receptors are involved in cancer metastasis as well as HIV-infection and were observed to form homo- and heterodimers [1]. The receptors CXCR4, CCR2 and CCR5 were shown to homo- as well as heterodimerize and the receptor association was reported to regulate the proteins' function [2]. In addition, the presence of membrane cholesterol was observed to modulate receptor activity [3]. The dimerization of these chemokine receptors was studied in absence and presence of cholesterol using thousands of molecular dynamics simulations on the microsecond timescale.

Our data suggests that the closely related CC chemokine receptors (transmembrane sequence similarity of 91%) homodimerize in similar patterns distinct from CXCR4. In addition, cholesterol bound to corresponding spots on CC chemokine receptors (primarily TM6 and TM7), while different binding positions for cholesterol were observed for CXCR4 (mainly TM1 and TM7). The presence of cholesterol especially modulated the homo- and heterodimerization of CXCR4 by largely blocking TM1 from engaging in dimer interactions, but inducing dimer conformations including TM4 via intercalating at the dimer interface [4].

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C.14 Spatial cytoskeleton organization supports targeted intracellular transport

Anne E. Hafner and Heiko Rieger

Theoretical Physics, Saarland University, Saarbrücken, Germany

The efficiency of intracellular cargo transport from specific source to target locations is strongly dependent upon molecular motor-assisted motion along the cytoskeleton. Radial transport along microtubules and lateral transport along the filaments of the actin cortex underneath the cell membrane are characteristic for cells with a centrosome. The interplay between the specific cytoskeleton organization and the motor performance realizes a spatially inhomogeneous intermittent search strategy. In order to analyze the efficiency of such intracellular search strategies we formulate a random velocity model with intermittent arrest states. We evaluate efficiency in terms of mean first passage times for three different, frequently encountered intracellular transport tasks: i) the narrow escape problem, which emerges during cargo transport to a synapse or other specific region of the cell membrane, ii) the reaction problem, which considers the binding time of two mobile particles within the cell, and iii) the reaction-escape problem, which arises when cargo must be released at a synapse only after pairing with another particle. Our results indicate that cells are able to realize efficient search strategies for various intracellular transport tasks economically through a spatial cytoskeleton organization that involves only a narrow actin cortex rather than a cell body filled with randomly oriented actin filaments.

C.15 The Mechanics of Vesicle Blebbing

Sebastian Hillringhaus, G. Gompper and D.A. Fedosov

Institute of Complex Systems, Forschungszentrum Juelich, Juelich, Germany

A broad range of in silico models (e.g. liquid or viscoelastic drop models) has been introduced to reproduce the complex mechanical properties of various cell types [1]. These models are used to understand and quantify experimental measurements. In this work, we employ a coarse- grained cell model which incorporates the membrane properties similar to the RBC-model [2] and an elastic inner mesh to include the cytoskeletal properties. The model is formulated in the framework of the dissipative particle dynamics simulation method. We investigate cell-blebbing in synthetic vesicles that are observed experimentally [3]. Cell-blebbing describes the dissociation of the membrane from the inner network, in this case as result of inner stress. The dissociated membrane will form a bubble within no actin network exists. We analyze different properties of the system in silico and link them to biological factors as concentrations of binding proteins and physical properties like the applied stress.

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C.16 Adhesion forces of spherical bacteria investigated by scanning force microscopy

L. Hofherr[1], N. Davoudi[1], J. Chodorski[2], C. Müller-Renno[1], R. Ulber[2], Ch. Ziegler[1]

[1]*Department of Physics and Research Center OPTIMAS, University of Kaiserslautern, Germany*
[2]*Institute of Bioprocess Engineering, University of Kaiserslautern, Germany*

Biofilms create a favorable environment for the embedded bacteria and are therefore of growing interest for technical systems such as biofilm reactors. To optimize the growth conditions for a biofilm, we investigated the influence of different environmental factors on the adhesion forces by single cell force spectroscopy. Besides different pH values, ionic strengths and contact times we also studied various surfaces and a gram-negative as well as a gram-positive bacterium.

The gram-negative seawater bacterium *Paracoccus seriniphilus* showed the strongest adhesion forces for acidic pH values and an increased ionic strength compared to the growth medium.

Further, we performed contact angle, zeta potential and scanning force microscopy measurements to link the change in adhesion forces of bacteria to the variation of environmental conditions and the resulting properties of the bacteria. These measurements proof that the results of the force spectroscopy experiments can be completely explained by the electrostatic forces between cell and surface.

C.17 Cell Protrusion and Retraction Driven by Fluctuations in Actin Polymerization: A Two-Dimensional Mathematical Model

Danielle Holz[1], Gillian L. Ryan[2] and Dimitrios Vavylonis[1]

[1]*Department of Physics, Lehigh University, 16 Memorial Drive East, Bethlehem PA 18105, United States, and*
[2]*Department of Physics, Kettering University, 1700 University Avenue, Flint MI 48504, United States*

Many cell types adhered to a 2D surface exhibit protrusion and retraction of their actin-rich lamellipodia even without translation. Traveling waves of protrusion have been observed, similar to crawling cells. The regular patterns of protrusion and retraction allow quantitative analysis for comparison to mathematical models. Excitable actin dynamics have been linked to the periodic fluctuations in leading edge position of XTC cells using a 1D model of actin dynamics [1]. This model was extended into 2D to include movement of a model membrane that protrudes and retracts due to changes in the number of free barbed ends of actin filaments near the membrane. Patterns of membrane protrusion and retraction can be reproduced if the polymerization rate at the barbed ends depends on the local concentration at the leading edge and the opposing force from the cell membrane. Both Brownian ratchet and switch-like force-velocity relationships between the membrane and load forces and actin polymerization rate were investigated. Both models were in qualitative agreement with experiments by the Watanabe group (Kyoto University). However, the switch-like model exhibited sharper behavior. The model generates predictions for the behavior of cells after local membrane tension perturbations.

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C.18 Multiscale Model of the Formin Homology 1 Domain Illustrates its Role in Regulation of Actin Polymerization

Brandon G. Horan[1] , Gül Zerze[2], Gregory L. Dignon[2], Young C. Kim[3], Dimitrios Vavylonis[1], Jeetain Mittal[2]

[1]*Department of Physics, Lehigh University, Bethlehem, PA, USA*
[2]*Department of Chemical and Biomolecular Engineering, Lehigh University, Bethlehem, PA, USA*
[3]*Center for Materials Physics and Technology, Naval Research Laboratory, Washington, DC 20375, USA*

Actin, indicated in numerous cellular processes, is primarily responsible for cytoskeletal structure. Highly regulated actin polymerization into filaments is key in these processes. Formin, a dimer-forming actin regulator, binds profilin to the polyproline tracks of the proline-rich of its believed flexible Formin Homology (FH) 1 domain. The FH2 domains wrap around the barbed end of the actin filament and elongates the filament processively. Profilin-actin complexes on FH1 domain are modeled to transfer to the barbed end; however, the mechanism is not known. Previous models of the FH1 domain have not captured sequence-specific effects such as the length and distribution of the polyproline tracks and possible variety in mechanosensitivity and response to bound profilin. To remedy this we perform all-atom molecular dynamics simulations of FH1 and show that FH1 is a typical intrinsically disordered protein (IDP), with the polyproline tracks forming high propensity poly-L-proline helices. We develop an alpha-carbon coarse-grained model [1] that retains the sequence-specificity of FH1 domain which is consistent with the IDP notion of FH1, and use this to study the FH1 domain in the context of its biological role. We use the coarse-grained model to investigate the response of FH1 to force and bound profilin.

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C.19 Forces for lateral detachment of bacterial cells from structured component surfaces

K. Huttenlochner[1], N. Davoudi[1], C. Schlegel[2], F. Pütz[1], L. Heimann[1], M. Huster[2], M. Bohley[3], C. Müller-Renno[1], J. C. Aurich[3], R. Ulber[2], C. Ziegler[1]

[1]Department of Physics and Research Center OPTIMAS, TU Kaiserslautern, Germany
[2]Institute of Bioprocess Engineering, TU Kaiserslautern, Germany and
[3]Institute for Manufacturing Technology and Production Systems, TU Kaiserslautern, Germany

The use of productive biofilms in biofilm reactors is a promising method for producing chemical substances [1]. For this, bacterial adhesion is a fundamental step for creating the biofilm. In our CRC 926 we develop structured component surfaces for improving bacterial adhesion. Shear forces in a flow bioreactor play an important role on bacterial attachment, which can be observed by Lateral Force Microscopy (LFM) [2]. Here we determined the number of moved bacteria on a surface when applying different lateral forces. Investigation of different structured surfaces shows a positive effect of the structures on bacterial attachment compared to an unstructured very smooth surface.

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C.20 Atomic Force Microscopy as a precision tool to study cell mechanics and adhesion

Jagoba Iturri, Alberto Moreno-Cencerrado and José Luis Toca-Herrera

Institut for Biophysics, Department of Nanobiotechnology, BOKU University for Natural Resources and Life Sciences, Vienna, Austria.

Atomic Force Microscopy (AFM), operated in Force Spectroscopy mode, has become a standard tool for studying mechanical properties of soft materials at the nanoscale by sample indentation experiments. In such conditions, the AFM tip is restricted to move perpendicularly to the sample of interest (Z), with a high accuracy in its XY positioning. Tip displacement occurs under controlled approach/retract speeds and maximum loads in contact. Furthermore, both the thermodynamic conditions and the type of specific/non-specific interaction to be characterized can be adapted on demand, either by temperature adjustment or by chemical modification of the measuring probe, respectively[1]. The capability of an AFM to accurately manipulate samples also permits direct quantification of cell–substrate adhesion forces by means of the so called "single-cell probe force spectroscopy", where a living cell is used as probe[2-3]. Appropriate analysis of the Force vs distance curves obtained allows extracting various mechanical parameters attending to the segment of the curve chosen: Young's modulus and stiffness (approach), maximum adhesion force (retract) and rheology-related stress relaxation and creep compliance –strain-(pause in contact)[4-5]. Combination of these complementary features ensures a rather complete characterization of the (bio)material of interest, as shown in this work.

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C.21 Exploring the basic mechanisms of bacterial contact formation and breaking: Combining AFM force spectroscopy & MC simulations

Karin Jacobs[1], Christian Spengler[1], Nicolas Thewes[1], Thomas Faidt[1], Friederike Nolle[1], Johannes Mischo[1], Frank Müller[1], Philipp Jung[2], Ludger Santen[3], and Markus Bischoff[2]

[1]Saarland University, Experimental Physics, 66041 Saarbrücken, Germany, and
[2]Institute for Medical Microbiology and Hygiene, Saarland University, 66421 Homurg/Saar, Germany
[3]Saarland University, Theoretical Physics, 66041 Saarbrücken, Germany.

Combining single bacterial probe force spectroscopy [1] with Monte Carlo (MC) simulations [2], a multitude of details on the bacterial adhesion process is gained [3,4]. As bacterial probes, we use cocci, e.g. *Staphylococcus aureus*. Already the form of the force/distance curve (FDC) upon approach of the bacterium to the solid is characteristic for the type of binding between the bacterial cell and a specific surface. On hydrophobic surfaces, the FDCs exhibit a pronounced snap-to-contact at a distance of ~50 nm from the surface, a process that can be eliminated by cutting or crosslinking proteinaceous components of the cell wall [2]. To mimic the experimental FDCs, MC simulations need to take ten thousands of macromolecules (simulated as elastic springs with a distribution of spring constants) into account to make contact via hydrophobic interactions to the surface. However, on hydrophilic surfaces, experimental FDCs display no snap-to-contact, and only a few tens of elastic springs are needed in the MC simulations to mimic the curves. The force to remove the bacterium from the hydrophilic surface is an order of magnitude smaller than on hydrophobic surfaces, where the hydrophobic effect plays the main role. Experimental determinations of the size of the contact zone of the bacterial cell suggest that adhesive force and contact area are not correlated [4]. Rather, differences in cell wall macromolecule composition determine the adhesive behavior.

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C.22 Microtubule tug-of-war and stochastic kinetochore oscillations

Jan Kierfeld and Felix Schwietert

Physics Department, TU Dortmund University, Dortmund, Germany

We investigate the cooperative dynamics of microtubules, which are elastically coupled to kinetochores in the mitotic spindle. The model includes the dynamic instability of microtubules, forces on microtubules and kinetochores from elastic linkers and, eventually, an external force on the kinetochore. We use stochastic simulations and analytical solutions of Fokker-Planck equations to first analyze one hemisphere of the mitotic spindle consisting of an ensemble microtubules coupled to one kinetochore under a constant external force. In simulations of this one-sided spindle model, kinetochore movement exhibits bistable behavior as a function of the applied force [1]. Solving the Fokker-Planck equations for the microtubule-kinetochore distance distribution, we derive bistable behavior and conditions for the occurrence of bistability analytically. This allows us to quantify the bistable regime in the parameter plane of linker stiffness and microtubule numbers. In the full two-sided spindle model, two such bistable systems are coupled in a tug-of-war. This leads to stochastic chromosome oscillations in metaphase, which have been observed in several experiments.

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C.23 Flows in Starfish Oocyte Cytoplasm Driven by Surface Contraction Wave

Nils Klughammer[1], Johanna Bischof[2], Péter Lénárt[2] and Ulrich S. Schwarz[1]

[1]Institute for Theoretical Physics, University of Heidelberg, Heidelberg, Germany and [2]Cell Biology and Biophysics Unit, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany

Meiotic divisions of starfish oocytes are closely related to surface contraction waves (SCWs) of which the exact function is unclear. Apart from generating large-scale deformations of the cell envelope, they also lead to hydrodynamic flows inside the cell. Both cell deformations and hydrodynamic flow can be measured with optical microscopy and quantified using image analysis.

We have developed an analytical continuum theory to predict the hydrodynamic flow from the experimentally measured cell deformations. This now can be compared with the experimental data giving us the possibility to study flow generation and to estimate properties of the cytoplasm, including its viscosity. It also allows us to predict the pressure field, that cannot be measured directly. Finally our results might be used to elucidate if the hydrodynamic flow is simply a physical consequence of the SCWs or also has a biological function, e.g. to distribute certain factors inside the large cell.

C.24 Tumor phenomenology in cell-based computer simulations

Edoardo Milotti[1], Sabrina Stella[1], and Roberto Chignola[2]

[1]*Department of Physics, University of Trieste, Via Valerio 2, I-34127 Trieste, Italy,*
[2]*Department of Biotechnology, University of Verona, Strada Le Grazie 15 - CV1, I-37134 Verona, Italy*

Cell-based computer simulations of tumor growth capture phenomena at many scales, both in time and in space. More importantly, cell-based simulations take into account events in individual cells – like mutations that lead to different phenotypes – that are subsequently amplified by cell-proliferation. These features lead to an increased computational complexity but they also allow to peek into the complicated dynamics of cancer and synthesize a nontrivial structural phenomenology of growing tumors. Here we describe our cell-based computer program for the simulation of tumor growth [1,2], and show how it has been exploited to obtain phenomenological models that bridge different space-time scales and help in understanding the biology of cancer [3-6].

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C.25 Protein gradients in single cells induced by "morphogen"-like diffusion

Saroj Kumar Nandi and Sam A. Safran

Department of Materials and Interfaces, Weizmann Institute of Science, Rehovot 7610001, Israel

One of the many ways cells transmit information within their volume is through steady spatial gradients of dierent proteins. However, the mechanism through which such single-cell gradients form is not yet fully understood. We rst demonstrate that one of the models for gradient formation, based on dierential diusion, is limited to proteins with large ratios of their diusion constants or to specic protein-large molecule interactions. We then introduce an alternative for gradient formation via the coupling of the proteins within a single cell with a molecule whose action is similar to that of morphogens in multi-cell assemblies; the \morphogen" is produced with a xed ux at one side of the cell. This coupling results in an eectively non-linear diusion degradation model for the \morphogen" dynamics within the cell; it is the non-linearity that leads to a steady state gradient of the protein concentration. We use a stability analysis to show that these gradients are linearly stable with respect to perturbations.

C.26 Essential dynamics of tubulin in a microtubular fragment

Alexandr Nasedkin and Jan Swenson

Department of Physics, Chalmers University of Technology, Gothenburg, Sweden

Microtubules are dynamical cell structures experiencing complex rearrangements during their growth and shrinkage [1]. Microtubular dynamics is associated with conformational changes in tubulin, which is a building block of the microtubule [2]. Naturally, tubulin interacts with multiple molecules and proteins. Motions responsible for protein functions are forming an essential conformational space. An analysis of such space helps to assign principal motions to functional properties, e.g mechanism of actions of anti-cancer drugs targeting tubulin [3].

In this work we employ the all-atom molecular dynamics simulations to follow the principle motions of tubulin molecules in a wall of the microtubule. Modelling system was prepared based on a minimal fragment of the microtubule. Simulations allow to follow and differentiate principle modes of individual tubulin units depending on their position in the microtubule, which in turn gives an insight into dynamics of both ends of the microtubule in particular.

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C.27 Propagation of dipoles in non-linear elastic media

Guglielmo Saggiorato and Martin Lenz

LPTMS, CNRS, Univ. Paris-Sud, Université Paris-Saclay, 91405 Orsay, France

How do forces propagate through complex media, such as the cytoskeleton? Previous works highlighted that dipoles applied to a non-linear network of fibers are distorted by the medium itself. At large distances the dipole is amplified and rectified always towards an effective contractile dipole independent on the nature of the applied dipole [1]. Indeed, under high-enough load fibers buckle and create a rope-like medium around the local dipole. One possible consequence for the cell is that the cytoskeleton can serve as an active regulator of the propagation of local forces (e.g. exerted by myosin) to upper scales. We generalize this result to all non-linear materials and for generic dipoles. We find that also neutral local dipoles (neither contractile nor extensile) are rectified, and that the rectification direction depends on the medium non-linear response, e.g. strain-softening or strainstiffening. This implies that the effect is not restricted to rope-like media only. Moreover two fundamentally different non-linear contributions are systematically present in a non-linear medium: geometrical and material ones. The rectification direction is tuned by the material non-linearities. The geometrical ones, instead, cannot be tuned and shift the threshold from contractile to extensile materials. Our results are validated by simulations with finite elements of a hyper-elastic material which interpolates between strain-stiffening and softening response.

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C.28 Optogenetically regulated biomaterials: novel microenvironments for studies in mechanotransduction

Shrikrishnan Sankaran,[1] Shifang Zhao,[1] Christina Muth,[1] Julieta Paez,[1] Aranzazu del Campo[1,2]

[1]*Dynamic Biomaterials, INM Leibniz Institute for New Materials, Campus D2 2, 66123 Saarbrücken, Germany*
[2]*Chemistry Department, Saarland University, 66123 Saarbrücken, Germany*

Cells sense, translate and react to mechanical stimuli from their microenvironment by linking specific membrane receptors and cytoskeletal structures to the extracellular matrix and neighboring cells. To study such phenomena, artificial interfaces displaying receptor-specific ligands have been developed.[1] A recent unique approach explores the concept of "living biointerfaces" involving genetically programmed prokaryotes to dynamically display relevant ligands involved in mechanotransductive cellular processes. Seminal studies have successfully demonstrated this principle using non-pathogenic L. lactis bacteria.[2] I will present a novel optogenetically regulated living biomaterials platform that enables to control, in situ, the presentation of receptor-specific ligands on a living biointerface using light. It is based on a special endotoxin-free strain of the most extensively engineered prokaryote, E. coli., genetically engineered to display a mammalian cell-adhesive ligand on its surface upon mild illumination. This platform is developed as a powerful academic tool to activate and regulate mechanotransduction processes.

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C.29 Cytoplasmic actomyosin contractions drive streaming in zebrafish eggs

Shayan Shamipour

Heisenberg group, Institute of Science and Technology Austria, Klosterneuburg, Austria

At the onset of zebrafish development, the egg is composed of a mixture of yolk granules (the food supply for the future larva) and cytoplasm from which the embryonic tissues will develop. For development to start, the cytoplasm and yolk granules segregate with all the cytoplasm accumulating at one side of the egg (animal pole) and the yolk granules on the other (vegetal pole). This process is called 'cytoplasmic streaming' as the cytoplasm flows to the animal pole of the egg, while the yolk granules remain in the vegetal pole. The goal of this project is to unravel the physical basis of cytoplasmic streaming within the egg.

Previous studies have speculated that reorganization of cortical actomyosin triggers cytoplasmic flows within the egg. By generating embryos lacking cortical actomyosin, we were able to show that cytoplasmic streaming also occurs in the absence of the cortical actomyosin network, arguing against a critical function of this network in generating cytoplasmic flows. Instead, we propose that contraction of a previously uncharacterized subcortical actomyosin network can drive this process.

C.30 Deriving the Drosophila gap gene system ab initio by optimizing information flow

Thomas R. Sokolowski[1], Aleksandra M. Walczak[2], Thomas Gregor[3], William Bialek[3], and Gašper Tkačik[1]

[1]*Institute of Science and Technology Austria (IST Austria), Klosterneuburg, Austria*
[2]*École Normale Supérieure, Paris, France*
[3]*Princeton University, Princeton, New Jersey, U.S.A.*

Spatio-temporal protein patterns are crucial for communicating information within and between cells. However, their ability to convey signals robustly is hampered by noise in gene regulation and biochemical transport. It remains largely unclear how nature orchestrates different biochemical noise control strategies to maximize information flow, especially in spatial scenarios. Here we take the approach of theoretically predicting the best gene-regulatory design of a developmental patterning system that optimizes transmission of relevant information, starting only from biophysical principles and without any fitting involved. To this end, we construct a generic spatial-stochastic model which allows for rigorous quantification of information flow in an ensemble of gene-regulatory units encoding a spatially distributed input signal in multiple downstream target outputs [1,2]. By optimizing information capacity over all relevant model parameters, we obtain predictions for the gene-regulatory architectures that maximize encoding of positional information in the output patterns [1,3]. We exemplify our approach by applying it to a paradigmatic developmental system, the gap gene patterns in the early development of the *Drosophila* fly [6]. The theoretically predicted optimal patterns are compared to high-quality experimental measurements of means and covariances of the gap gene products [4,5], using the same model framework for inference.

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C.31 Positional information readout in Ca^{2+} signaling

Wasnik Vaibhav

Living cells respond to spatial signals. Signal transmission to the cell interior often involves the release of second messengers like Ca^{2+} . They will eventually trigger a physiological response by activating kinases that in turn activate target proteins through phosphorylation. Here, we investigate theoretically how positional information can be accurately read out by protein phosphorylation in spite of rapid second messenger diusion. We nd that accuracy is increased by binding of the kinases to the cell membrane prior to phosphorylation and by increasing the rate of Ca^{2+} loss from the cell interior. These ndings could explain some salient features of conventional protein kinases C.

C.32 A microfluidic method for capsule and cell sorting based on mechanical properties

Doriane Vesperini, Ilyesse Bihi and Anne Le Goff

Laboratoire de Biomécanique et Bioingénierie, Université de Technologie de Compiègne UTC, Compiègne, France

Cell mechanical properties depend on their differentiation stage or pathologies such as cancer or infections. Sorting cells according to their stiffness is thus particularly interesting in tissue engineering and diagnostic applications [1]. We propose a microfluidic device that consists of a cylindrical obstacle located at the end of a rectangular straight channel [2]. Upstream of the obstacle, a flow--focusing module centers cells on the obstacle. Downstream of the obstacle, a diffuser ends on 5 symmetrical outlets. Trajectories in the diffuser depend on several parameters, such as cell size, deformability and velocity. Stiff micro--objects are more deflected than soft ones. We already have proven the efficiency of our device for larger micro--objects such as capsules [3]. It is a passive, non--destructive, and sensitive system. We have now downscaled the microfluidic device to adapt its geometry to cell sizes.

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C.33 Altering nanoparticle uptake pathway by engineering cell membrane stiffness

Shengnan Xiang[1], Melika Sarem[1, 2, 3], Samveg Shah[1], and V. Prasad Shastri[1]

[1]*Institute for Macromolecular Chemistry, University of Freiburg, Freiburg, 79104 (Germany)*
[2]*BIOSS Centre for Biological Signaling Studies, University of Freiburg, Freiburg, 79104 (Germany)*
[3]*Helmholtz Virtual Institute on Multifunctional Biomaterials for Medicine, Kantstr. 55, Teltow, 14513 (Germany)*

Nanomaterials such as nanoparticles (NPs) and liposomes; are taken up by cells via endocytosis, a process that involves deformation of cell membrane [1]. The deformability of cell membrane is dictated by lipid bilayer phase behavior as this can influence the stiffness/softness of the bilayer [2]. Using liposomes exhibiting different phase behavior, we have discovered that energy dependent endocytic uptake of liposomes is related to the stiffness of the liposome. Since, cell membranes can be modified by liposomes through lipid transfer [3], we theorized that liposomal treatment of cells could alter membrane softness/stiffness and therefore influence endocytosis of NPs. Using breast epithelial tumor cells (MD-MBA-231) as a model system we have shown that engineering of cell membrane phase behavior through liposomal pre-treatment can alter dynamin mediated uptake of polymeric NPs. Since there is evidence that in cancer cells dysregulation of lipid synthesis and metabolism alters mechanical properties of cell membranes[4], liposomal treatment opens a new avenue to improve nanomedicines uptake in cancer cells.

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C.34 Influence of vinegar on biofilms formation *in situ*

Yong Liu and Matthias Hannig

Clinic of Operative Dentistry, Periodontology and Preventive Dentistry. Saarland University. Homburg, Germany

Objectives:

The study was intended to elucidate the efficacy of commercially available vinegar on *in situ* pellicle formation and biofilms.

Methods:

In situ biofilm formation was carried out over 3 min and 24 h on bovine enamel slabs mounted in individual splints for 3min and 24h. After rinsing with vinegar, all the samples were analyzed via BacLightTM viability assay, SEM and TEM. The samples with only water rinsing served as control groups.

Results:

In part one, vinegar rinsing reduced the outer globular layer of the pellicle and resulted in formation of a network-like subsurface pellicle. In part two, vinegar caused a significant reduction in bacterial viability and disruption of the mature biofilm. After vinegar rinsing, total bacteria amount of saliva samples decreased remarkably within 30 min, and bacterial viability reduced even 120 min in both biofilm and saliva.

Conclusion:

This *in situ* study reveals that rinsing with vinegar for 5 s alters the pellicle layer resulting in subsurface pellicle formation. Furthermore, vinegar rinsing will destruct mature (24-h) biofilms, and significantly reduces the viability of planktonic microbes in saliva, thereby decreasing biofilm formation.

Poster Abstracts

P.1 Bidirectional Non-Markovian Exclusion Processes

Robin Jose, Chikashi Arita and Ludger Santen

Theoretical Physics, Saarland University, Saarbrucken, Germany

The totally asymmetric simple exclusion process (TASEP) is a basic tool to examine transport properties of molecular motors along a filament in a cell, which is one of the most fundamental interacting particle systems on a lattice. Usually it is a Markov process, i.e. the distribution of waiting time between two adjacent stochastic events is of exponential, but recently a TASEP with non-Markovian waiting times was introduced [1]. In our presentation, we introduce some generalizations of the non-Markovian TASEP to two-species of particles moving in opposite directions. We show simulation results of the models, and discuss a phase transition between flowing and condensation states.

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P.2 On the growth of helical pipe protrusions out of lipid bilayers interacting with ESCRT-III subunits

Luca Barberi and Martin Lenz

LPTMS, CNRS, Univ. Paris-Sud, Université Paris-Saclay, 91405 Orsay, France

ESCRT-III is a cytosolic protein complex necessary for membrane remodeling in a number of cellular processes, ranging from cytokinesis [1] to multivescicular body biogenesis [2] and viral budding [3]. Despite its importance, we still have a limited knowledge on the specific contribution of each of its subunits in deforming lipid bilayers. One of these, Snf7, has been observed to polymerize on membrane substrates in the shape of spirals [4], whose out-of-plane buckling could, theoretically, drive an invagination dynamics [5]. Recent unpublished observations by our collaborators from the Roux Lab in Geneva have shown how the addition of two further ESCRT-III subunits, namely Vps2 and Vps24, can make helical pipe membrane protrusions bud away from the cytoplasm. As they bind to a Snf7 spiral, Vps2 and Vps24 could directly influence its preferred curvature and torsion, making it grow out of the plane of the membrane to which it sticks and leading to the formation of the observed helical protrusions. In order to validate this prediction, we developed a model of polymerized membrane and present some preliminary results on the mechanically stable configurations of such system.

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P.3 Substrate stiffness differentially alters cell proliferation and apoptosis during tissue morphogenesis

Saikat Basu , Sabyasachi Sutradhar and Raja Paul

Department of Solid State Physics, Indian Association for the Cultivation of Science, Kolkata, India

A key challenge in cell and tissue morphogenesis is to learn how the evolving tissue pattern is guided and maintained by a suitable balance between cell proliferation and apoptosis. Considering these two processes strongly coupled with cell's interaction with the extracellular matrix (ECM), adhesion dependent active mechanosensing of local stiffness is crucial. Adhered cells both create and sense tension in the extracellular matrix and change the environment to favorable condition in which they can survive. In this project, we aim to understand how various tissue patterns are generated when proliferation and apoptosis of cells are altered by varying the physical and mechanical properties of the ECM. Using an *in silico* elastic network in two dimensions, we simulate the composite *cell-ECM* structures with varying structural and mechanical integrity of ECM and review characteristic features of the tissue upon successive cell proliferation and apoptosis. Our data suggests that, in general, a uniformly rigid ECM facilitates proliferation, while apoptosis is predominant on a compliant ECM; more precisely, cell's viability is a function of the local stress. Cells in a tissue, simultaneously undergoing proliferation and apoptosis rapidly grow in locally stressed regions forming spike like structures on a rigid substrate. On the other hand, regions lacking stress become devoid of cells; a feature commonly observed during tumorigenesis. Additionally, we find that recovery of a scratch wound is delayed for cells harbored on a compliant or (and) in a highly collagen depleted ECM. Our model predictions concur with available experimental results.

P.4 Novel roles of KDEL receptor at the cell surface of mammalian and yeast cells

Björn Becker[1], M. Reza Shaebani[2], Domenik Rammo[1], Ludger Santen[2], Manfred J. Schmitt[1]

[1]Molecular and Cell Biology, Department of Biosciences and Center of Human and Molecular Biology (ZHMB), Saarland University, D-66123 Saarbrücken, Germany
[2]Department of Theoretical Physics, Saarland University, D-66123 Saarbrücken, Germany

Several microbial A/B toxins including cholera toxin and the yeast viral K28 toxin contain a KDEL-like motif at their cell binding subunit which ensures retrograde toxin transport through the secretory pathway. A key step in the invasion process is the initial binding of each toxin to distinct plasma membrane (PM) receptors that are parasitized by the toxins and utilized for cell entry. Recently, we could demonstrate that eukaryotic KDEL receptors (KDELRs) are not only present in membranes of the secretory pathway but also in the PM where they are capable to bind and internalize KDEL-bearing cargo proteins. By analyzing A/B toxin binding and internalization in conjunction with confocal and TIRF microscopy we could identify the KDEL receptor Erd2p as plasma membrane receptor of the viral K28 killer toxin in yeast [1]. Since human KDELR homologs were shown to be fully functional in yeast and capable to restore toxin sensitivity in a Δ*erd2* knock-out, KDELR-mediated toxin uptake from the cell surface is likely to occur also during A/B toxin invasion of mammalian cells. In this respect, we could already show that the addition of an ER-retention motif to a fluorescent variant of ricin toxin A chain is *in vivo* recognized by PM-localized KDELRs as KDEL-cargo and subsequently internalized from the cell surface. In a combined experimental and theoretical approach we showed that cargo binding induces a dose-dependent cellular response that results in receptor cluster formation at and subsequent internalization from the PM, associated and counteracted by anterograde and microtubule-assisted receptor transport to preferred docking sites [2].

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P.5 Transmembrane Protein-Induced Membrane Curvature

Christoph Kluge and Rainer A. Böckmann

Computational Biology, Department of Biology, Friedrich-Alexander University Erlangen-Nürnberg, Germany

The local curvature of cellular membranes can function as a sorting mechanism for transmembrane proteins, e.g. by accumulation in regions of matching spontaneous curvature (SC), as shown recently for potassium channel KvAP and water-pore AQP0 by Aimon et al. [Aimon (2008), Dev. Cell, 28(2), 212-218]. However, the direction of the reported SC as well as the molecular background could not be addressed experimentally yet. Using coarse-grained and atomistic molecular dynamics simulations, we analyzed the levels of spontaneously induced curvature for the homologous potassium channel Kv 1.2/2.1 Chimera (KvChim) and AQP0 when embedded in unrestrained POPC lipid nano-discs. Coarse-grained results are in excellent agreement with the experiments, at values of 0.036 nm^{-1} and -0.019 nm^{-1} induced by KvChim and AQP0, respectively. Furthermore, the direction of curvature can be retrieved directly from the simulations. Atomistic simulations of both systems show a SC comparable to the coarse-grained results, and allow for detailed investigation of its origin, especially in terms of protein-lipid interactions. Here, uneven distribution and organization of POPC lipids at the interface of KvChim establishes a basal positive curvature, which is then further modified by the dynamics of the protein.

P.6 Characterization of Mesenchymal Stem Cells and Microcarriers

N. Davoudi[1], N. de Isla[2], C. Müller-Renno[1], E. Olmos[2], Ch. Ziegler[1]

[1]Department of Physics and Research Center OPTIMAS; University of Kaiserslautern; D-67663 Kaiserslautern, Germany
[2]Lorraine University, 54000 Nancy, France

Stem cells are undifferentiated cells with the ability to differentiate into various specialized cells if appropriate growth conditions are provided. The use of mesenchy-

mal stem cells (MSCs) in cell therapy (1) and regenerative medicine (2) has been limited by their cell source quantity. Since MSCs are only available in small numbers in the human body, they need to be isolated and expanded. Microcarriers have been employed successfully for their expansion (3). The main goal of this study is to determine the correlation of the properties of the microcarriers (such as roughness, zeta potential and hydrophobicity) to their interaction which MSCs. Therefore, three microcarrier beads (cytodex-1, plastic and plastic plus) are characterized with scanning force microscopy, powder contact angle measurement, and X-ray photoelectron spectroscopy. The interactions (adhesion and elasticity) of the microcarriers and the MSCs will be measured by scanning force microcopy (SFM).

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P.7 v-SNARE-based protein-lipid interactions catalyze membrane fusion

M. Dhara[1], M. Mantero[1], R. Mohrmann[2], D. Bruns[1]

[1]Saarland University, Homburg, Germany
[2]Zentrum für Human und Molekularbiologie, Saarland University, 66424 Homburg/ Saar, Germany

Ca^{2+}-triggered fusion of vesicles with the plasma membrane enables neurotransmitters release, underlying information processing in the central nervous system. Overcoming electrostatic repulsion, shedding of hydration shells, bending of membranes etc. put an energetic toll on the fusion process. While this energy threshold is actively surmounted by membrane bridging interactions between vesicular and target SNARE (*soluble N-ethylmaleimide-sensitive factor attachment protein receptors*) proteins, SNARE: phospholipids interactions may help catalyzing membrane merger. In this work, we have investigated the role of vesicular SNARE synaptobrevin-2 (syb-2) and phospholipid interactions in Ca^{2+}-triggered neurotransmitter release. Using a combination of photolytic 'uncaging' of intracellular Ca^{2+} with membrane capacitance mea-

surement and analysis of single amperometric spikes in chromaffin cells, we found that structural flexibility of the syb-2 transmembrane domain (TMD) positively affects the extent of membrane fusion and rate of cargo release from single granules. Amperometric measurement of chromaffin granule fusion also showed that membrane-active agents that either alters curvature (e.g. lysophosphatidyl choline, oleic acid) or membrane fluidity (e.g. cholesterol) regulate fusion. Furthermore, we could show that the slow fusion pore expansion in syb-2-TMD mutants can be rescued with membrane-active agents, demonstrating that the protein and lipid functions converge on the same intermediate steps to promote exocytosis. Thus, our results demonstrate that SNARE TMDs play an active role in the fusion process that goes beyond simple anchoring of the protein, and their functional pas de deux with lipids determines Ca^{2+} triggered neurotransmitter release.

P.8 Comprehensive measurements of salivary pellicle thickness formed at different intraoral sites on Si wafers and bovine enamel

Johanna Dudek[1], Sabine Güth-Thiel[1], Ines Kraus[1], Hubert Mantz[2], Karin Jacobs[2], Matthias Hannig[1]

[1]*Clinic of Operative Dentistry, Periodontology and Preventive Dentistry, University Hospital, Saarland University, Homburg/Saar and*
[2]*Experimental Physics, Saarland University, Saarbrücken, Germany*

The salivary pellicle is a thin acellular film formed on orally exposed surfaces by adsorption of macromolecules from the oral fluids and serves as a protective layer in the maintenance of oral health. It has been shown that loss of minerals and enamel surface alterations after acid attack was less pronounced on enamel covered with a pellicle as compared to those without pellicle [1]. The pellicle's protective properties have been related to its composition, formation time and thickness [2]. Therefore pellicle thickness measurements are an important tool helping to understand how exogenous manipulations may influence pellicle formation. In the present study we determined the kinetics of the in situ pellicle thickness formation at different intraoral sites and investigated how pellicle formation occurs in different individuals. To address the kinetic aspect, the thickness of the in situ pellicle was determined after formation periods of 3, 30 and 120 min. The thickness of the pellicle was either measured on

Si wafers by ellipsometry or on bovine enamel by transmission electron microscopy (TEM). We found a physiological important rapid pellicle formation phase within the first minutes and a slow pellicle formation phase between 30 and 120 min. Furthermore, our results identify significant inter-individual differences both for the pellicle thickness and for the formation kinetics.

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P.9 A phase-field approach for studying actin-wave driven cell migration

Nicolas Ecker[1], Luiza Stankevicins[2], Franziska Lautenschläger[2,3] and Karsten Kruse[1]

[1]Theoretical Physics and Biochemistry Departments, University of Geneva, Switzerland
[2]INM Leibniz Institute for New Materials, Saarland University, Saarbrücken, Germany
[3]Experimental Physics, Saarland University, Saarbrücken, Germany

Cells migrate to search for nutrients as well as during immunological responses and developmental processes. Migration is driven by the actin cytoskeleton. How the network is organized in this process, is still poorly understood. Spontaneous actin waves have been observed in a large number of different cell types and present an attractive concept to understand cytoskeletal orchestration during migration. We introduce a mean-field description of actin waves. The actin network is confined to an evolving cellular domain by means of a phase field. We find erratic motion due to the formation of spiral waves and compare these findings to experiments.

P.10 Using atomic force microscopy and live cell imaging to unravel new functions of the extracellular adherence protein Eap of *Staphylococcus aureus*

Janina Eisenbeis, Henrik Peisker, Christian S. Backes, Nicolas Thewes, Markus Greiner, Christian Junker, Eva C. Schwarz, Markus Hoth, Karin Jacobs, Markus Bischoff

Institute for Medical Microbiology and Hygiene (IMMH), Homburg, Germany

Staphyloccocus aureus is a major human pathogen, and a common cause for superficial and deep seated wound infections. The pathogen expresses a multitude of virulence factors which facilitate attachment to various eukaryotic cell structures and modulate the host immune response. One of these factors is the extracellular adherence protein Eap that is secreted by *S. aureus* into the host milieu to exert a number of adhesive and immune evasive functions. Eap is also known to contribute to a delayed wound healing of *S. aureus* infected wounds. In order to better understand the latter phenomenon, we analyzed here the impact of Eap on keratinocyte morphology and behavior by atomic force microscopy and live cell imaging. We could show that treatment of keratinocytes with Eap resulted in cell morphology changes as well as a significant reduction in cell proliferation and migration. Specifically, we found that Eap-treated keratinocytes changed their appearance from an oblong to an astral-like shape, accompanied by decreases in cell volume and cell stiffness, and exhibited significantly increased cell adhesion. Additionally, we found that Eap interfered with growth factor-stimulated activation of the MAPK pathway that is known to be responsible for cell shape modulation, induction of proliferation and migration of epithelial cells.

P.11 Fluoridation of hydroxyapatite – Time dependence and protective properties

Thomas Faidt[1], Andreas Friedrichs[1], Christian Zeitz[1], Samuel Grandthyll[1], Michael Hans[2], Matthias Hannig[3], Frank Müller[1] and Karin Jacobs[1]

[1]Experimental Physics, Saarland University, Saarbrücken, Germany
[2]Functional Materials, Saarland University, Saarbrücken, Germany
[3]Clinic of Operative Dentistry, Periodontology and Preventive Dentistry, Saarland University Hospital, Homburg, Germany

The application of fluoride containing products to protect tooth enamel from caries is daily practice for many decades. However, to this day little is known about the time dependence of fluoride uptake in hydroxyapatite (HAP) which is the mineral component of human enamel. In our study, we used highly dense HAP pellet samples as a model system for the crystallites of tooth enamel [1]. To investigate the time dependence of the fluoride uptake, samples were exposed to a fluoride solution (NaF, 500 ppm) for different times. XPS depth profiling revealed a saturation behavior both for the overall amount of fluoride taken up by the sample and for the thickness of the formed fluoridated layer [2]. We found that the maximum thickness of the fluoridated layer is about 13 nm. To explore the efficacy of such an ultrathin layer as a protective shield against acid attacks, we used AFM to determine the etching rates of untreated and fluoridated HAP samples. In spite of very low fluoride concentrations in the fluoridated samples, our results show a strong reduction of the etching rate after fluoride treatment.

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P.12 Expression regulation by a methyl-CpG binding domain and the incorporation of non-canonical amino acids in an *E. coli* based, cell-free TX-TL system

M. Schenkelberger[1], S. Shanak[2,4], M. Finkler[1], E. G. Worst[1], V. Noireaux[3], V. Helms[4], and A. Ott[1]

[1]*Saarland University, Department of Experimental Physics, Saarbrücken, 66041, Germany*
[2]*Arab American University-Jenin, P.O.Box 240, Palestine*
[3]*University of Minnesota, School of Physics and Astronomy, Minneapolis, 55455, USA*
[4]*Saarland University, Center for Bioinformatics, Saarbrücken, 66041, Germany*

Cytosine methylation plays an important role in the epigenetic regulation of eukaryotic gene expression. The methyl-CpG binding domain (MBD) is common to a family of eukaryotic transcriptional regulators. How MBD, a stretch of about 80 amino acids, recognizes CpGs in a methylation dependent manner, and as a function of sequence, is only partly understood. Here we show, using an *E. coli* cell-free expression system, that MBD from the human transcriptional regulator MeCP2 performs as a specific, methylation-dependent repressor in conjunction with the BDNF (Brain-Derived neurotrophic factor) promoter sequence [1]. We give a simple kinetic model that describes the repression and fits the experimental data [1]. The *E. coli* cell-free expression system can also be used for the incorporation of non-canonical amino acids [2]. We present first results as well as future plans.

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P.13 New Strategy to Study a Single SNARE Mediated Membrane Fusion Event

Jean-Baptiste Fleury[1], Jose Nabor Vargas[1], Kewin Howan[2], Ralf Seemann[1,3], Andrea Gohlke[2,4], James E. Rothman[4], and Frederic Pince[t2,4]

[1]Experimental Physics, Saarland University, Saarbrücken, Germany, [2]Laboratoire de Physique Statistique, Ecole Normale Supérieure, 75005 Paris, France [3]Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany [4]Department of Cell Biology, School of Medicine, Yale University, CT 06520 New Haven, USA

We present an approach to explore the properties of a single SNARE mediated membrane fusion event in a microfluidic chip. In a first step, a single free standing lipid membrane is generated at a defined position with the Droplet Interface Bilayer technique (DiB). In a second step, we inject a solution of divalent cations (Calcium, Ca2+) and small unilamellar vesicles functionalized with T-SNARE proteins (T-SUVs) around the planar membrane using a volume controlled flow. The presence of calcium mediates the direct fusion of the vesicles with the planar membrane, which is incorporating the proteins into the membrane. In a third step, we remove the calcium and the T-SUVs with a buffer solution. After this washing step, a solution of small unilamellar vesicles functionalized with V-SNARE proteins (V-SUVs) is injected around the planar membrane. And finally, we study single fusion event with good optical and electrical access.

P.14 Actin cortex dynamics and structure upon myosin II inhibition

Daniel Flormann[1], Kevin Kaub[1], Zahra Mostajeran[1] , Emmanuel Terriac[1] and Franziska Lautenschläger[1,2]

[1] Cytoskeletal Fibers, INM Leibniz Institute for New Materials, Saarbrücken, Germany
[2]Faculty of natural and technical Sciences, University of Saarland, Saarbrücken, Germany

In the frame of the project A9, Structure and dynamics of the cell cortex before, during and after adhesion, the cortex of cells has to be characterized in both initial (suspended) and final (adhered) states. The dynamics of the cortex is measured by FRAP (Fluorescence Recovery After Photobleaching) while its structure is investigated by electron microscopy. The first results will be presented in this poster. Via analysis of the FRAP experiments, it is possible to extract some insights of the content of the cortex, especially the ratio between long formin mediated actin filaments and short Arp2/3 mediated ones. Cells were also treated with Para-nitro blebbistatin (a non-photodegradable version of the well-known blebbistatin) in order to inhibit the motor protein myosin II. Changing the activity of the motor protein modifies, as expected, the dynamics of the entire cortex. More surprisingly, we show here that the changes between suspended and adhered states go in opposite directions: while the turnover rate of actin decreases in adhered cells, it is increased in the suspended case.

P.15 Vascular Adaption Dynamics – An old idea probed with modern techniques

Thierry Fredrich and Heiko Rieger

Theoretical Physics, Saarland University, Germany

The complex relationship between vascular network morphologies, their role in nutrient or drug transport and the influence of solid tumors is focused by our research.

Traditionally the radii of a hierarchical transport networks such as the vasculature are observed to follow the formula of Murray which can be derived from basic physical principles. Despite of giving a good estimate on what to expect, the formula provi-

des no further biological insides.

In the past, Secomb et. al. [1] proposed a biologically motivated scheme to dynamically regulate blood vessel radii where the topology as well as the metabolic demand of surrounding healthy tissue is taken into account. So far this approach was used to describe observed data from rat mesentry networks. High Performance Computing together with modern evolutionary optimization algorithms [2] enables us to apply the proposed adaptation scheme to artificial vasculatures created by our in house software package called "tumorcode".

Preliminary results show that Murrays law is not strictly fulfilled in the scope of that model. We present corresponding hydrodynamic distributions and study the influence on the oxygen distribution. The long term goal would be to understand the hierarchical signalling process and its malfunction caused by tumors.

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P.16 Influence of actin dynamics on speed and persistence of immune cells

Peter Fries[1], Franziska Lautenschläger[1,2], Karsten Kruse[1,3]

[1]*Department of Physics, Saarland University, Saarbrücken, Germany*
[2]*INM Leibniz Institute for New Materials, Saarbrücken, Germany*
[3]*Université de Genève, Geneva, Switzerland*

The actin cytoskeleton plays a crucial role in motility of living cells. We investigated the role of different actin associated proteins (e.g. Arp2/3, formin) in the one dimensional movement of neutrophil precursor cells in microfluidic channels. Stochastic simulations were performed to fit the data to a persistent random walk. We observed

that inhibition of actin associated proteins alters intrinsic properties of the process. It could be shown that another important factor in the cell's movement is its probability of stopping which could be altered with specific drugs affecting the actin cytoskeleton (CK666, SMIFH2, Y27632). Also they altered persistence time and length, as well as speed. Further, we performed high resolution experiments in a TIRF microscope and recorded the actin dynamics. The data showed that actin polymerization waves at the cell's front were present and could be altered by inhibiting actin associated proteins. A special focus laid on the actin cytoskeleton during the directional change of a cell. We investigated the hypothesis that as long as no polymerization waves were present the two sides of the cell competed until one side formed polymerization waves which caused the cell to move into the corresponding direction.

P.17 Adhesion of cellulose binding modules – a single molecule study

A.Griffo[1], B. Rooijakkers[2], M. B. Linder[2], P. Laaksonen[1]

[1]*Department of nanostructures and materials*
[2]*Department biotechnology, Aalto University, Espoo, Finland*

In Nature, certain organisms, such as fungi, have developed special enzymes namely cellulases, containing protein domains that are able to attach the actual enzyme to cellulose selectively [1]. Similar protein domains also exist at the interfaces of biological composites such as nacre and can play very important role in bringing about adhesion between the components of hybrid materials. Here, we will quantify the binding ability of cellulose binding modules (CBMs) from the enzymes Cel7A from the fungus T. Reesei, by measuring the strength of adhesion on cellulosic surfaces. In fact, being highly abundant and renewable, cellulose is an interesting option for nanocomposites [2].
In details single molecule force spectroscopy technique (SMFS) is employed into the understanding of the binding affinity at molecular level. The protein of interest is attached covalently to the tip by a multistep covalent functionalization process.

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P.18 Feedback, trafficking and morphogen scaling

Zena Hadjivasiliou

University of Geneve, Geneve, Switzerland

During development tissues develop into organs of stereotyped size and shape. Morphogens are secreted from discrete regions in developing organs and form spatial concentration gradients that guide gene activation, pattern formation and tissue growth. Morphogen gradients scale with tissue size, ensuring that morphological patterns remain proportionate in organs of different size. How key molecular players ensured morphogen scaling is not clear. Motivated by observations of the BMP-type growth factor **Decapentaplegic (Dpp)** in the fly wing, we explore the potential role of local feedback driven by Dally/Dpp interactions in morphogen scaling.

P.19 Lipid-free, pure-protein bilayers and vesicles from native fungal hydrophobins

Hendrik Hähl[1], Nabor Vargas[1], Michael Jung[1], Friederike Nolle[1], Nathalie Tritz[1], Alessandra Griffo[2,3], Päivi Laaksonen[2,3], Geza Szilvay[2], Michael Lienemann[2], Karin Jacobs[1], Ralf Seemann[1], and Jean-Baptiste Fleury[1]

[1]*Department of Experimental Physics, Saarland University, 66123 Saarbrücken, Germany*
[2]*VTT Technical Research Centre of Finland Ltd., 02150 Espoo, Finland*
[3]*Department of Materials Science and Engineering, Aalto University, 02150 Espoo, Finland*

The compartmentalization of an aqueous solution by semi-permeable membranes is of utmost importance in biology. Typically, the matrix of these membranes is composed by bilayers made from phospholipids. Thereby, the amphiphilic character of the lipids is necessary for bilayer formation. Since phospholipids are limited in their variety in mechanical and biochemical properties, alternative building blocks are sought for specialized applications. Proteins seem to be ideal candidates promising biocompatibility and versatility via genetic engineering. A special type of amphiphilic proteins, hydrophobins, appears to be particularly suited. These proteins occur natu-

rally in filamentous fungi being involved in, e.g., sporulation or adhesion. In this study, bilayers made purely from hydrophobins were created using a microfluidic platform. The ability of these bilayer to be formed between any type of fluid compartments, be it gas, water, or oil is demonstrated, which renders hydrophobins much more versatile than lipids. Via microfluidic jetting, vesicles were formed from these different types of bilayers. In the case of vesicles in aqueous surrounding, gramicidin-A ion channels could be inserted into the bilayer allowing the transport of monovalentions [1] [2]. Thus, these vesicles are the first example of vesicles with lipid-free, artificial bilayers containing inserted functional proteins.

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P.20 Modeling of T-Cell polarization

Ivan Hornak and Heiko Rieger

Theoretical Physics, Saarland University, Germany

The polarization of T-Cell is a key part of many fundamental biological processes. It takes place during the destruction of the target cell by T-Cell, and, therefore, it is one of the primary processes of the immune system. The polarization was experimentally observed, but its inner dynamics and key features remained poorly understood. We developed a physical model of microtubules and their organizing center that is able to realistically simulate the rotation of the microtubule structure and repositioning of the microtubule organizing centre towards the immunological synapse. The output of the model is in compliance with the experimental observations. We use the model to clarify rudimentary aspects of the repositioning, such as biphasic movement of the centrosome. The model is also used for parameter estimation.

P.21 Optoregulation of 3D cellular microenvironments

Qiyang Jiang, Aleeza Farrukh, Julieta I. Paez and Aránzazu del Campo

INM Leibniz Institute for New Materials, Saarbrücken, Germany

Light-responsive hydrogels are promising platforms to mimic the dynamic properties of natural cellular microenvironments and investigate cellular processes and responses to physiological and pathological changes. Reported examples mainly deal with the incorporation of photocleavable chromophores to change the mechanical, chemical and topological properties of hydrogels upon light exposure both in 2D and 3D cell cultures using well established o-nitrobenzyl chemistry. A major limitation of this group for realizing microenvironment changes in situ with 3D resolution is its poor two-photon absorption cross-section, leading to cell photodamage and loss of function.

We present new biocompatible hydrogel designs that allow 3D patterning of areas with distinct adhesive ligands upon light exposure in the presence of cells. The gels contain ligands modified with two-photon sensitive chromophores and have initially no activity. Upon laser scanning, the chromophore is removed and the ligand becomes activated at selected positions within the gel. Site-selective activation allows us to define patterns with specialized areas within the gel and guide the regeneration of patterned tissues.

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P.22 Trapping in and escape time from tree-like structures of neuronal dendrites

Robin Jose, Christian Sand, Ludger Santen, and M. Reza Shaebani

Department of Theoretical Physics, Saarland University, 66041 Saarbrücken, Germany

The branching morphology of neuronal dendrites in advanced nervous systems allows the neuron to interact simultaneously with several neighbors and additionally

controls the transmission time of signals. Although it is expected that alterations in dendritic morphology induced by neurodegenerative disorders or aging directly influence the neural functions, it is not yet clear how transport properties of signals are affected by changes in key geometrical parameters. We present a model for stochastic transport inside dendritic trees and obtain exact analytical expressions for escape times from such complex structures, which identify the contributions of the extent of the tree, the bias induced by hierarchical variations of branch diameter, and the adsorption probability at biochemical cages. The analytical predictions are in remarkable agreement with simulation results. We moreover study how presence of disorder in the structure influences the first passage time statistics, and verify that volume exclusion does not affect the exponential nature of the tail behavior of the escape time distribution.

P.23 A Biomaterials Platform to Decouple Cell-Matrix and Cell-Cell Forces

Aleeza Farrukh,[1] Desna Joseph [1,2], Roshna Vakkeel, [1] Aránzazu del Campo[1,2]

[1]*INM Leibniz Institute for New Materials. Campus D2 2,Saarbrücken, Germany*
[2]*Department of Chemistry, Saarland University, Saarbrücken, Germany*

Cells apply forces to communicate with other cells and with the extracellular matrix. For this purpose cells form physical contacts with neighbouring cells or the ECM using membrane adhesive receptors. Over the last years different methods have been developed to measure cell forces, like traction force microscopy, micropipettes, micropillar arrays AFM etc. None of these methods allows independent measurement of cell-cell and cell-ECM forces independently and in a monolayer-like geometry with spatially segregated cell-ECM and cell-cell receptor complexes, as it occurs in natural epithelium.
We present a biomaterials platform to mimic the epithelial cell niche and spatially confine cell-cell and cell-ECM interactions using PAAm Gels with a novel design. They allow site-independent immobilization of cadherin and fibronectin peptidtidomimetics and independent modulation of their mechanical link. These platforms represent advanced substrates for measuring cellular forces.

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P.24 Initial adhesion of biofilm forming pathogens to central venous catheters: the role of blood serum proteins

Philipp Jung[1], Gubesh Gunaratnam[1], Christian Spengler[2], Nicolas Thewes[2], Karin Jacobs[2] and Markus Bischoff[1]

[1]*Institute of Medical Microbiology and Hygiene, University of Saarland, Homburg, Germany*
[2]*Experimental Physics, University of Saarland, Saarbrucken, Germany*

Microbial biofilms formed on implanted medical devices such as central venous catheters (CVC) are of major clinical importance. The interaction of biofilm forming microorganisms with the implanted material is a key factor in disease pathogenesis. Although a wealth of information exists on how major biofilm forming pathogens, such as *Staphylococcus aureus* and *Candida albicans*, adhere to clinically relevant implant materials, only little is known about how body fluid components that rapidly cover the implanted material will influence these initial adhesion processes. Hence, we aimed here to study by single cell force spectroscopy whether and how blood serum influences the initial adhesion of S. aureus and *C. albicans* to CVC material.
First results indicate that adhesion of both species is affected by blood serum. While S. aureus cells brought into contact with the CVC surface displayed a mean adhesion force of ~1.5 nN to this type of material, bacterial cells preincubated in serum adhered to the CVC with a mean adhesion force ≤0.5 nN. *C. albicans* yeast cells, on the other hand, adhered more firmly to the CVC when preincubated in blood serum, probably due to the formation of an initial hyphae that is induced by the presence of blood serum proteins.
Both findings indicate that host factors are likely to have a marked impact on the microbial adhesion to medical devices.

P.25 Vertex modeling of epithelial domes and tissue superelasticity

Sohan Kale[1], Ernest Latorre[1,2], Xavier Trepat[1,2] and Marino Arroyo[1,2]

[1]*Universitat Politècnica de Catalunya-BarcelonaTech, Barcelona 08028, Spain*
[2]*Institute for Bioengineering of Catalonia, Barcelona 08028, Spain*

Epithelial tissues are often curved into three dimensional shapes that enclose a pressurized lumen. Furthermore, during development and adult life these tissues can be highly stretched. However, the mechanics of epithelial monolayers under these conditions has not been quantitatively examined. Using soft micropatterned substrates we produce epithelial domes with controlled size and basal shape. By measuring 3D deformations of the substrate we obtain a direct measurement of epithelial tractions and luminal pressure. Tension in the freestanding epithelium is then mapped by combining measured luminal pressure and tissue curvature. Over time-scales of hours, we track tissue tension while epithelial domes reach nominal strains of 300%. Remarkably, we find that tissue tension reaches a plateau. Furthermore, despite the fact that the dome is subjected to uniform tension, the areal strain of individual cells can differ by more than one order of magnitude, with some superstretched cells reaching areal strains close to 1000%. To understand these observations, we develop a 3D vertex model [1,2]. We first note that a conventional 3D vertex model with constant junctional tension captures the tensional plateau under large stretches. However, when implemented computationally, this model does not replicate the cellular strain heterogeneity. We hypothesize that, as stretched cells increase their surface area by several fold, shortage of cytoskeletal components may lead to cell softening. We develop a model observing the limited amount of cortical material, which captures the tensional plateau and the cellular strain heterogeneity. According to this model, cells exhibit a non-convex multi-well energy landscape, and tissues accommodate stretch at constant tension by developing a mixture of cells in high- and low-strain phases, all of which are landmark features of superelasticity [3].

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P.26 Development of microtentacles in suspended cells upon inhibition of myosin

K. Kaub[12], E. Terriac[12], D. Bahr[1], L. Santen[1], F. Lautenschläger[12]

[1]*Physics Department, Saarland University, Saarbrücken, Germany*
[2]*Cytoskeletal Fibers, INM Leibniz Institute for New Materials, Saarbrücken, Germany*

Circulating tumor cells (CTCs) form microscopic tentacles (microtentacles or McTN), that are enriched with microtubules. Previous studies suggest that McTN may play an important role in the reattachment of metastatic CTCs within the microvasculature [1]. We observed the formation of similiar tentactles in vitro in suspended non-cancerous cells upon inhibition of myosin. Furthermore we observed softening in these cells as well; this phenomenon may be closely related to the ability of metastatic tumor cells to squeeze through the narrow microvasculature [2].
Our work focuses on the McTN and their formation in suspended non-cancerous cells upon myosin inhibition in vitro. The goal of this project is to understand how the McTN are formed and how the cortical composition influences their formation. We observed that myosin inhibition impacts the cortex in regards to the dynamical properties of cortical actin. Thus we ask if the change in dynamics of cortical actin serves as a prerequisite for the formation of McTN.

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P.27 Monte Carlo lattice modelling of a bilayer system

F. Keller, D. Hakobyan, A. Heuer

Westfälische Wilhelms-Universität Münster, Münster, Germany

Recently, a lattice model has been developed which allows one to describe the properties of lipid bilayer mixtures, containing DPPC and/or DLiPC [1]. It was introduced to examine the local phase separation and aggregation behavior of the respective lipids. The free energy functional is based on the lipid interaction enthalpy and lipid conformational chain entropy. All contributions can be extracted from short atomistic simulations. The model approach has proven to be able to correctly reproduce phase separation behavior and predict melting temperatures of gel phases for the lipid binary mixtures.

As cholesterol plays a crucial role in the dynamics of lipid bilayers, especially being prominent for its property to form the basis of lipid rafts, we present an extension of the lattice model by incorporation of cholesterol. We have to deal with different challenges, related, e.g., to the different sizes of cholesterol and DPPC/DLiPC. Adding cholesterol to the model will allow one to gain deeper insight into the fundamental mechanics of lipid raft formation and the basics of lipid-cholesterol interaction.

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P.28 Photoactivatable Hsp47: An optogenetic tool to regulate collagen assembly & tumor microenvironment

E. S.Khan[1, 2] , J. I. Paez[1],S. Sankaran[1], I. M. Weiss[3], A del Campo[1,2]

[1]*INM Leibniz Institute for New Materials, Saarbrücken, Germany*
[2] *Saarland University, Saarbrücken, Germany*
[3] *Universität Stuttgart, Stuttgart, Germany*

Molecular chaperones are folding modulators that play a central role in the conformational quality control of the proteome by interacting with, stabilizing and remodeling a wide range of specific proteins or non-native polypeptides. In pathological conditions like cancer a class of molecular chaperones called Heat shock proteins(Hsp's) causes chaperonopathies. Hsp47, a 47 kDa endoplasmic reticulum-resident heat shock protein involved in collagen maturation and assembly, has recently been discovered to regulate the tumor microenvironment by promoting expression of factors responsible for tumor cell proliferation, invasion and angiogenesis. In this contribution, we present a optogenetic strategies for developing photoactivatable Hsp47, and demonstrate the possibility of photoregulation of collagen assembly & tumor microenvironment related implications in a controlled manner.

P.29 P(3,5)P2 lipid binding-induced activation of the human two-pore channel 2

S.A. Kirsch[1], A. Kugemann[2], A. Carpaneto[4], N. Larisch[2], A. Schambony[3], T. Studtrucker[2], P. Dietrich[2] and R.A. Böckmann[1]

[1]*Computational Biology,*
[2]*Molecular Plant Physiology,*
[3]*Developmental Biology, Department of Biology, University of Erlangen-Nürnberg, Germany.*
[4]*Institue of Biophysics, National Research Council, Genova, Italy.*

Two Pore Channels (TPCs) are intracellular ion channels that are widely expressed in eukaryotic cells. Depending on the host cell, they are involved in diverse processes like the cellular cation and pH homeostasis, Ebola virus infection and cancer cell

migration. The gating mechanism and regulation of these channels are therefore of strong interest. It was shown that TPC1 of Arabidopsis thaliana gets activated in a Ca2+ and voltage dependent manner. Furthermore, patch-clamp experiments with wild type and truncated variants demonstrated that the C-terminus of AtTPC1 is an indispensable player for channel activity. In contrast, the homologous TPC2 of humans is gated open upon addition of phosphoinositides (PI(3,5)P2), however, the exact binding site and the relation to channel activation are unknown. To investigate the mode of channel activation of AtTPC1 and hTPC2 we combined experimental techniques and molecular dynamics simulations at the coarse-grained and atomistic level. Results demonstrated that AtTPC1 subunits interact via their C-terminal regions, and PI(3,5)P2 lipids tend to bind to predominately positively charged sub-regions of hTPC2. Further experiments will show if these homologues share common features in the gating mechanism.

P.30 Proteomic analysis of *in-situ* initial biofilm

Simone Trautmann[1], Lilia Lemke[1], Claudia Fecher-Trost[2], Ahmad Barghash[3], Matthias Hannig[1]

[1]Clinic of operative Dentistry, Periodontology and Preventive Dentistry, Saarland University, Homburg, Germany
[2]Experimental and Clinical Pharmacology and Toxicology, Saarland University, Homburg, Germany
[3]Center for Bioinformatics, Saarland University, Saarbrücken, Germany

The dental biofilm is generated by a continuous adsorption process of macromolecules and afterwards also microorganisms from saliva to the tooth surface. The initial, proteinaceous biofilm protects the tooth surface from mechanical damages and prevents demineralization due to the acids. The objectives of the current study were to investigate and to compare the individual proteomic profile of the in-situ initial biofilm and saliva. For biofilm formation bovine enamel specimens were mounted on splints and exposed in the oral cavity for 3 min. The in-situ initial biofilm and corresponding saliva of five subjects were collected and analyzed separately by mass spectrometry. An innovative chemical elution protocol combined with an optimized nano-LC-HR-MS/MS analysis was applied. A tremendous number of 736 different proteins was identified in the initial biofilm, exceeding all known biofilm protein quantities.

Biggest part of the proteins is derived from the low molecular weight range fraction of the salivary proteins. Most proteins exhibit binding, catalytic and enzyme regulatory activity according to the classification by molecular function categories based on Gene Ontology annotation. Distribution patterns of molecular weight and molecular function are similar between biofilm and saliva in all samples, despite individual differences of proteomic profile.

P.31 Interpenetrating Polymer Network Hydrogels with Multiple Local Stiffnesses

Bin Li, Colak Arzu, Roland Bennewitz and Aránzazu del Campo

INM Leibniz Institute for New Materials, Saarbrücken, Germany

Cells sense and respond to the mechanical properties of the extracellular matrix (ECM) at different time and length scales. Synthetic interpenetrating networks (IPNs) can be used to mimic the natural structures of ECM[1-3]. In this project, IPNs with independently crosslinked "soft" and "rigid" networks are prepared by using star-PEG/poly(ethylene-glycol diacrylate) mixtures through free radical polymerization and orthogonal polymerization methods. The macroscopic properties of IPNs are investigated, for example, water uptake and elasticity of swollen hydrogels. The local mechanical properties of the individual network can be controlled by the polymerization degree, the star-arm number and length, as well as the crosslink degree of both networks. High-resolution atomic force microscopy (AFM) is used to study the local mechanical property of the IPNs. The two networks are functionalized individually with different ligands, chemically functionalized AFM tip is used, for example, streptavidin-biotin complex. Cell behaviors on IPNs presenting both soft and stiff networks are individually modified with cell adhesive ligands are investigated, for example, cell spreading, focal adhesion, and stress fibers formation and maturation. We hypothesize that IPN architectures can present a variety of different mechanical signals at cellular mechanosensing levels.

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P.32 Space-Time Controlled DNA Cargo Delivery Performed by Active Janus Droplets

Menglin Li[1] Martin Brinkmann[1], Ignacio Pagonabarraga,[2], Ralf Seemann[1], and Jean-Baptiste Fleury[1]

[1]Experimental Physics, Saarland University, Saarbrücken, Germany,
[2]Universitat de Barcelona, Barcelona, Spain

Droplets made of a water/ethanol mixture in a continuous squalane/monoolein solution self-propel and evolve in up to three stages depending on droplet composition. With the different evolution stages also the propulsion mechanism as well as the corresponding hydrodynamic flow field change. In the first stage the droplets release ethanol and absorb surfactant molecules which leads to a phase separation of the water/ethanol/monoolein mixture and the formation of Janus droplets composed of a water–rich leading droplet and an ethanol–rich trailing droplet. The appearance and duration of the different stages can be controlled by the ethanol concentration in the droplets. Upon phase separation, DNA added to the initially formed droplets can be precipitated into the ethanol-rich droplet. Taking advantage of the specific swimming properties of the droplet in each stage and the adhesion properties of the ethanol– and water–rich droplets, we can control whether the cargo will be delivered at specific target locations. We can further control the timeframe and maximal distance of cargo delivery with the surfactant concentration in the continuous phase, the chemical composition of the droplets, and the droplet size. (Submitted)

P.33 Probabilistic analysis of apoptosis and necrosis in cancer cells induced by natural killer cells

E. Maikranz[1],C. Backes[2], C. Kummerow[2], M. Hoth[2] , H. Rieger[1]

[1]Department of Theoretical Physics, Saarland University, D-66123 Saarbrücken, Germany
[2]Department of Biophysics, Saarland University, D-66421 Homburg, Germany

Cytotoxic T lymphocytes and natural killer (NK) cells are the main cytotoxic killer cells of the human body to eliminate pathogen-infected or tumorigenic cells. They can kill target cells via the release of cytolytic molecules, which leads to necrosis or

apoptosis or induce apoptosis via binding to Fas receptors. Experimentally Backes et al. (unpublished) have observed, that the killing mechanism employed by a single NK cell varies in time and the sequence of the killing mechanisms varies among different cells of a population. Whether these variations indicate the existence of different NK cell phenotypes, or whether it is a purely probabilistic phenomenon is unknown. We rely on experimental data for these time sequences to model the observed sample of killing sequences as realizations of one or more independent stochastic processes. Each process represents different NK cell phenotype with different killing characteristics. We find that a model with one stochastic process suffices to reproduce the experimental data, and compute from maximum likelihood considerations the optimal parameter set for the observed data.

P.34 Bacterial adhesion on nanostructured surfaces

Friederike Nolle[1], Johannes Mischo[1,] Christian Spengler[1], Nicolas Thewes[1], Markus Bischoff[2,] Karin Jacobs[1*]

[1]Department of Experimental Physics, Saarland University, Saarbrücken, Germany
[2]Institute for Medical Microbiology and Hygiene, Saarland University, Homburg/Saar, Germany
**Corresponding author: k.jacobs@physik.uni-saarland.de*

Bacterial biofilm formation reduces the effect of antibiotics, which is one of the main reasons for the mandatory removal of infected implants from the body. Therefore, the prevention of biofilm formation or material specifications that result in the death of adhering bacteria without vitiating somatic cells is considered key in medical implant development. Our experiments aim at characterizing bacterial adhesion strength and viability of S. aureus. As the subsurface composition causes distinct changes in the adhesion forces due to a variation of the long-range van der Waals force, the adhesion on surfaces with varying nano-roughness but constant surface chemistry can be reduced to geometry constraints. Comparing hydrophobic and hydrophilic substrates of identical roughness reveal the influence of short-range, e.g. hydrophobic, forces on bacterial adhesion. The influence of roughness and hydrophobicity on cell viability was evaluated after each single cell AFM force spectroscopy and flowchamber experiment conducted.

P.35 Towards employing fluorescence anisotropy to measure the binding constant of hybridizing oligonucleotide DNA strands

Mina Mohammadi-Kambs, Albrecht Ott

Biologische Experimentalphysik, Universität des Saarlandes, saarbrücken, Germany

Fluorescence anisotropy provides a sensitive tool to measure the binding constant between two interacting molecules and has been used in case of ligand-protein or protein-DNA interaction. Here we use fluorescence anisotropy to determine the binding constant between two DNA strands. One of them is labeled with a fluorophore. The fluorophore is excited with polarized light. The emission polarization anisotropy depends on the rotational diffusion of the fluorophore during its excited state. If one strand binds to another, the anisotropy changes due to the changes in mobility of the fluorophore. We first designed a setup and then measured the binding constant among several 16 bp DNA strands, including different number of mismatches in different positions.

P.36 Theoretical modeling of kinesin and dynein gliding assays

Gina Monzon[1], Lara Scharrel[2], Stefan Diez[2] and Ludger Santen[1]

[1]*Department of Theoretical Physics, Saarland University, Saarbrücken, Germany and* [2]*B CUBE, Center for Molecular Bioengineering, Technical University Dresden, Dresden, Germany*

Inside the cell, cargo needs to be transported in a controlled, well targeted manner over long distances. The intracellular transport is performed by molecular motors walking on cytoskeletal filaments. Here we focus on microtubule-based long-range transport carried out by anterogradely directed kinesin and retrogradely directed dynein motors.
In close collaboration with the experiment we use theoretical modeling to investigate kinesin and dynein gliding assays with the objective of understanding their collective behavior inside the cell.

Our experimental results point out that contrary to kinesin motors, dynein motors need the collective to walk processively.
On the base of earlier studies of motor driven transport [1], we introduce a model where single dynein motors perform unbiased motion until they activate each other by tension.

[1] Sarah Klein, Cécile Appert-Rolland, and Ludger Santen. EPL (Europhysics Letters), 107(1):18004 (2014).

P.37 Topology preservation of disease-specific gene-regulatory subnetworks

Maryam Nazarieh[1,2], Hema Sekhar Reddy Rajula[1] and Volkhard Helms[1]

[1]*Graduate School of Computer Science, and*
[2]*Center for Bioinformatics, Saarland University, Saarbruecken, Germany*

Detecting differential expression (DE) of genes between normal and disease tissues is a common approach to get mechanistic insight into disease processes. Unfortunately, various bioinformatics methods for identifying such DE genes yield quite different results. Here, we used four bioinformatics tools to process RNA-Seq data taken from TCGA for matched tumor and normal samples of liver cancer and breast cancer patients. The overlap between the sets of significant DE genes was only 26 % in liver cancer and 28 % in breast cancer. Then, we constructed regulatory sub-networks involving transcription factors, microRNAs, and target genes that we predicted with our TFmiR web server [1] from the four sets of DE genes. We also identified both hotspot degree genes and a minimum set of dominator nodes using our integer linear programming approach described earlier [2]. Interestingly, we found that the topology of the regulatory networks constructed using TFmiR for the different sets of DE genes was highly similar with respect to hub degree nodes and dominator nodes. This suggests that key genes identified in regulatory networks derived from DE genes may give more insight into disease processes than simply inspecting the lists of DE genes.

[1] M. Hamed, C. Spaniol, M. Nazarieh, V. Hems, Nucleic Acid Res 43, gkv418 (2015).
[2] M. Nazarieh, A. Wiese, T. Will, M. Hamed, V. Helms, BMC Systems Biology 10, 88 (2016).

P.38 Regulation of glycolytic oscillations by the dynamics of intracellular water

Lars F. Olsen, Henrik S. Thoke[1,2], Sigmundur Thorsteinsson[2]
Roberto P. Stock[1] and Luis A. Bagatolli[1,3]

[1]Center for Biomembrane Physics (MEMPHYS) and
[2]Institute for Biochemistry and Molecular Biology, University of Southern Denmark, Campusvej 55, DK5230 Odense M, Denmark.
[3]Yachay EP and Yachay Tech, Yachay City of Knowledge, 100650 Urcuquí-Imbabura, Ecuador

We have explored the coupling of dynamics of intracellular water with metabolism in yeast cells. Using the polarity sensitive probe 6-acetyl-2-dimethylaminonaphthalene (ACDAN) we could show that glycolytic oscillations in the yeast *S. cerevisiae* BY4743 wild type strain are coupled to the Generalized Polarization function of ACDAN, which measures the ability of intracellular water to reorient in response to the excited state dipole of the probe. We analyzed the oscillatory dynamics in the wild type and 24 mutant strains with mutations in glycolytic, mitochondrial and vacuolar enzymes/ATPases, as well as proteins involved in actin polymerization and microtubule formation. Using fluorescence spectroscopy, we measured the amplitude and frequency of the metabolic oscillations and linked them to the ACDAN GP in the resting state of all 25 strains. The results show that there exist a lower and an upper threshold of ACDAN GP beyond which oscillations do not occur. The link between glycolytic oscillations and the ACDAN GP value also holds when ATP synthesis or the integrity of the cell cytoskeleton is perturbed. Our results represent the first demonstration that the dynamic behavior of a metabolic process can be, directly or indirectly regulated by a cell-wide physical property: the dynamic state of intracellular water. Our experimental data can be backed up by a mathematical model.

P.39 Spindle pole focusing is controlled by a buckling instability

David Oriola[1,2,3] , Johannes Baumgart[2,3], Frank Jülicher[2,3], Jan Brugués[1,2,3]

[1]Max Planck Institute of Molecular Cell Biology and Genetics,
[2]Center for Systems Biology Dresden, Pfotenhauerstraße 108, 01307, Dresden, Germany
[3]Max Planck Institute for the Physics of Complex Systems, Nöthnitzerstraße 38, 01187, Dresden, Germany

The mitotic spindle is a dynamic self-organized structure consisting of microtubules and other associated proteins. The bipolar shape of the structure is essential for the proper segregation of sister chromatids to the two daughter cells. Indeed, the inhibition of motor proteins in the spindle is known to lead to dramatic morphological changes in size and shape [1]. Although the interplay of molecular motors such as Dynein or Kinesin-5 are known to control spindle pole focusing, the underlying physical and molecular mechanisms are poorly understood. Here we use an active liquid crystal description to understand spindle shape and we find that stresses at the spindle poles control a buckling instability. Contractile stresses are found to close spindle poles whereas extensile stresses tend to open them. We hypothesize that molecular motors at the poles set a net active stress that controls the buckling transition. Finally, we are currently testing our predictions in meiotic Xenopus laevis egg extract spindles by means of fluctuation analysis, laser ablation and biochemical perturbations.

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P.40 Visualizing single subunits of ORAI channels with STEM to study stoichiometry dependence on activation status

Diana B. Peckys [1], Niels de Jonge [3, 4], Barbara A. Niemeyer [1], and Dalia Alansary [1]

[1]*Molecular Biophysics, Saarland University, Homburg/Saar, Germany*
[3]*INM Leibniz Institute for New Materials, Saarbrücken, Germany*
[4]*Department of Physics, Saarland University, Saarbrücken, Germany*

The dynamics of intracellular Ca^{2+} signals govern a wide variety of cellular functions. Especially for long lasting processes cells rely on the so-called store-operated Ca^{2+}entry pathway. STIM1 proteins in the endoplasmic reticulum (ER) sense a decrease of the Ca^{2+} concentration, then react by clustering and trapping of ORAI1 proteins, located in the plasma membrane, to form functional Ca^{2+} channels in close apposition to the ER. ORAI channel stoichiometry may thus change during different functional states (i.e. at rest, and during channel activation). The assembly and stoichiometry of ORAI channels remains a matter of debate, and dimeric, tetrameric as well as hexameric assembly was reported. To solve this question we reached out for the visualization of single ORAI ion channel subunits, by using HA-tag labeling with fluorescent nanoparticles in combination with a novel correlative light- and electron microscopy technique [1]. Contrasting conventional approaches using extraction of proteins from their native environment of the plasma membrane we thus studied ORAI1 stoichiometry in intact cells in their liquid state. Therefore we first generated cells without endogenous ORAI1 expression, using the CRISPR/Cas9 approach, and different HA-tagged ORAI1 constructs, including concatenated ORAI1 proteins, which allow us to calculate our labeling efficiency. Labeled cells at rest and after activated Ca^{2+} influx, were then subjected to recording of STEM images with 2 nm resolution. Finally, statistical analysis of automatically measured distances between thousands of individually labeled proteins, was used to study ORAI1 stoichiometries under different conditions.

[1] D.B. Peckys, et al, Microsc. Microanal. 22(4), 902-912, (2016).

P.41 Calcium-Redox feedback loop in immune cells: New players and regulatory mechanisms

Girish Ramesh, Lukas Jarzemblowski, Dalia Alansary, Alina Gilson, Annette Lis, Barbara A. Niemeyer

CIPMM, Saarland University, Homburg, Germany

Ca^{2+} release-activated Ca2+ (CRAC) channels were originally identified as store-operated highly selective Ca2+ channels in primary rat mast cells and Jurkat T cells [1] [2], but have since been found in virtually all cell types. While STIM1 and Orai1 constitute the main subunits of CRAC channels in lymphocytes, other cell types contain different combinations/ratios of Orai1, Orai2 or Orai3 and STIM1 or STIM2. We are interested in physiological and pathophysiological regulation of CRAC channels by environmental factors such as oxidation, as well as by posttranslational alterations. During inflammation, immune and surrounding cells encounter environments rich in reactive oxygen species (ROS), generated by phagocytes such as monocyte-derived cells. We have shown in the past that Orai3 is critical in controlling the ROS sensitivity of store-operated Ca^{2+} entry (SOCE) and using MD simulations solved the mechanism of ROS induced inhibition of Orai1 [3]. The physiological role of Orai2, however, remains enigmatic. In T cells Orai2 can act as a negative regulator of SOCE but its role in other cell types with predominant Orai2 expression is unclear. In addition, the molecular differences governing STIM-Orai2 interfaces and thereby controlling Ca2+ are unclear. Data concerning novel regulatory mechanism will be presented.

[1] M. Hoth, and R. Penner: Depletion of intracellular calcium stores activates a calcium current in mast cells. Nature 355, 353-356 (1992).
[2] Zweifach A, Lewis RS.: Mitogen-regulated Ca2+ current of T lymphocytes is activated by depletion of intracellular Ca2+ stores. Proc Natl Acad Sci U S A. ; 90: 6295-9 (1993).
[3] Alansary D, Schmidt B, Dörr K, Bogeski I, Rieger H, Kless A, Niemeyer BA. Thiol dependent intramolecular locking of Orai1 channels. Sci Rep.; 14; 6:33347 (2016).

P.42 Determination of chlorhexidine by MALDI-TOF MS after application of different chlorhexidine formulations

Bashar Reda[1], Klaus Hollemeyer[2], Simone Trautmann[1], Dietrich A. Volmer[2], Matthias Hannig[1]

[1]*Clinic of Operative Dentistry, Periodontology and Preventive Dentistry, Saarland University, Homburg, Germany and*
[2]*Institute of Bioanalytical Chemistry, Saarland University, Saarbrücken, Germany*

Aim: To determine chlorhexidine (CHX) retention in the oral cavity after application of different CHX formulations.
Methods: Five volunteers used different formulations of CHX: mouth rinses, spray, and toothpastes. After application, 2µL samples were taken from the saliva, buccal mucosa as well as in situ formed enamel pellicle at six time-points within 12h. Retention of CHX was measured using MALDI-TOF mass spectrometry.
Results: The CHX retention at the oral mucosa was higher than in saliva. The retention of CHX in the oral cavity after mouth rinsing or spray application was higher than after using of the toothpastes. The concentrations of CHX at the oral mucosa maintained at a level of micrograms per millilitre 12h after mouth rinsing, 10h after spray and 2h after toothpaste application.
Conclusion: There was a significant difference in CHX retention between the mouth rinse, spray, and toothpaste. The novel used method offered excellent quantification limits and readily permitted quantification of CHX.

P.43 Profilin 1 reduces CTL migration and survival under high tension

Renping Zhao, Rouven Schoppmeyer, Yan Zhou, Eva C. Schwarz, Markus Hoth, Bin Qu

Biophysics, Centre for Integrative Physiology and Molecular Medicine, School of Medicine, Saarland University, 66421 Homburg, Germany

In a solid tumor, inter-tension is very high. It was reported that high tension affected cell morphology and gene expression of cancer cells. However, it is unknown whether high tension plays any role on cytotoxic T lymphocytes (CTL) and the potential mechanism. Here, we used different concentrations of collagen to mimic various tensions. High tension reduced the searching efficiency and survival of CTL. This might explain the difficulty of immune cell killing target cells in solid tumor tissues. Our previous work has revealed that in patients with pancreatic cancer, profilin 1 (PFN1), essential for F-actin elongation, was decreased in peripheral CD8+ T cells (Schoppmeyer and Zhao et al. unpublished). Therefore, we further investigated the role of PFN1 on CTL under different tension in vitro. We found that F-actin was accumulated at the site of nuclear deformation, and the accumulation was increased under higher extracellular tension. Down-regulation of PFN1 further reduced the migration velocity and persistence, as well as the survival of CTL compared with control CTL under high tension.

P.44 Modelling the motility of Cytotoxic T Lymphocytes inside infected lymph nodes

Zeinab Sadjadi[1] ,Stephan Halle[2] and Michael Meyer-Hermann[1]

[1]*Helmholtz Center for Infection Research, Braunschweig, Germany and*
[2]*Institute for Immunology, Hannover Medical School, Hannover, Germany*

Cytotoxic T Lymphocytes detect and kill infected cells in lymph nodes. The underlying mechanisms of this process are however still unclear. The results of 2- photon microscopy experiments in vivo have shown different migration patterns and processivities of CTLs during search and killing processes[1]. We aim to understand the possible roles of chemotaxis, T cells cooperativity during killing, and fibroblastic reticular net-

work on the dynamics and search strategy of CTLs inside a lymph node. We develop a two-state persistent random walk model for the motion of CTLs during search and killing phases. Four different realizations of experiments are of particular interest: no virus infection (control), virus infection without cognate antigen MCMV-2D, virus infection without direct presentation MCMV-3D, virus infection with direct antigen presentation of target cells MCMV- 3D-ΔvRAP. By tuning the parameters of the analytical model to each of the realizations we reproduce the observed dynamics of CTLs, which enables us to study the role of key parameters on search efficiency and killing.
[1] Stephan Halle et al., Immunity 44, 233(2016).

P.45 Reaction-diffusion model for Orai1-STIM1 interaction during CRAC channel formation

Barbara Schmidt[1], Barbara A. Niemeyer[2] and Heiko Rieger[1]

[1]Theoretische Physik, and [2]Molekulare Biophysik, Universität des Saarlandes, 166123 Saarbrücken and 266421 Homburg, Germany

Ca^{2+}-release activated Ca^{2+} (CRAC) channels are the major pathway of store-operated Ca^{2+} entry to activate immune cells. Upon Ca^{2+} -release from the ER stromal interaction molecules (STIM) in the ER membrane and Orai proteins in the PM interact and form CRAC channels, whose Ca^{2+} -conductance can be modulated by extracellular reactive oxygen species (ROS). We formulate a reaction-diffusion model to quantify the STIM-Orai interaction during CRAC channel formation and analyze different Orai1 channel stoichiometries and different ratios of STIM1 and Orai1 in comparison with experimental data. We incorporate the inhibition of Orai channels by ROS into our model and calculate its contribution to the CRAC channel amplitude.

P.46 Human profilin 1 is a negative regulator of CTL mediated cell-killing and migration

Rouven Schoppmeyer[1] , Renping Zhao[1] , He Cheng[2-4] , Chen Liu[2-4] , Xiao Zhou[1] , Eva C. Schwarz[1] , Yan Zhou[1] , Arne Knörck[1] , Mohamed Hamed[5,6] , Gertrud Schwär[1] , Shunrong Ji[2-4] , Liang Liu[2-4] , Jiang Long[2-4] , Volkhard Helms[5] , Markus Hoth[1] , Xianjun Yu[2-4] , Bin Qu[1]

[1] Biophysics, Center for Integrative Physiology and Molecular Medicine, Faculty of Medicine, Saarland University, 66421 Homburg, Germany
[2]Department of Pancreatic and Hepatobiliary Surgery, Fudan University Shanghai Cancer Center, P.R. China
[3]Department of Oncology, Shanghai Medical College, Fudan University, P.R. China
4 Pancreatic Cancer Institute, Fudan University, Shanghai 200032, P.R. China
[5] Center for Bioinformatics, Saarland University, 66041 Saarbrücken, Germany
[6] Institute for Biostatistics and Informatics in Medicine and Ageing Research, University of Rostock, 18057 Rostock, Germany

Actin dynamics are essential for proper cytotoxic T lymphocyte (CTL) functions e.g. migration, formation of the immunological synapse (IS) and killing through lytic granules (LGs). Profilin1 (PFN1) plays a major role in control of actin dynamics yet the functional role of PFN1 in CTL remained elusive. We identified PFN1 as the only PFN isoform expressed in primary human CTL. We identified PFN1 as a negative regulator of CTL-mediated target cell elimination and LG release. During CTL migration, PFN1 modulates cell average velocity, protrusion formation patterns and protrusion sustainability whilst cell migration persistence and emergence and retraction rates of protrusions are not significantly affected. Mimicking a tumor microenvironment in vitro, we show that PFN1 downregulation enhances invasion of CTL into a 3D matrix and that CTL do not show decreased viability in a hydrogen peroxide enriched microenvironment. CTL of pancreatic cancer patients showed a substantially decreased PFN1 expression compared to healthy individuals, emphasizing a potential relevance of PFN1 in cancer. In summary, we conclude that PFN1 is a negative regulator of CTL-mediated cytotoxicity with potential impact on tumor-related functionality of CTL.

P.47 Record Statistics of Non-Markovian Random Walks

M. Reza Shaebani, Nicolas Mooij, and Ludger Santen

Department of Theoretical Physics, Saarland University, Saarbrücken, Germany

Understanding the statistics of extreme events in stochastic processes is of crucial importance in a variety of fields, ranging from sport, to climates and biology. While record statistics of a few types of Markovian random walks, such as ordinary and biased walks, have been studied, there is much less known about the extreme events in non-Markovian random walks. To understand the impact of carrying a memory of the previous steps on the record statistics, we investigate a few types of non-Markovian random walks with different types of memories: persistent, elephant and Alzheimer random walks. Persistent walks carry a short-range memory of the previous directions of motion. We show how this correlation between the turning angles of the walker influences the short time behavior of the number of records and their ages. We show that the persistency changes the frequency of the records and affects the crossover time to asymptotic ordinary diffusive dynamics. We also study elephant walks, which carry the whole memory of the previous steps. We verify that, in a specific region of the phase space of the elephant walk's parameters, the record statistics differ from those of an ordinary random walk. Finally, an Alzheimer walker follows the same dynamics as an elephant walker, with the difference that its memory is limited to a fraction of the previous steps of motion. We show how this limited range of the memory leads to a strong bias and influences the record statistics.

P.48 Intracellular Calcium dynamics during T cell polarization and activation

Bhavesh Soni and Heiko Rieger

Department of Theoretical Physics, Saarland University, Saarbrücken, Germany

Processes as diverse as proliferation, fertilization and memory are controlled by Ca^{2+} signaling. However, how this versatility is regulated in terms of rate, magnitude and spatiotemporal patterning of Ca^{2+} signals is largely unknown. It has been observed that heterogeneity of Ca^{2+} concentration in the cell results in various global Ca^{2+} signals, which in succession control, for example, neuronal function and gene expres-

sion. However, much less is known about the relocation of channels, pumps and organelles which lead to the development of local Ca^{2+} micro-domains. Considering the context of T-cell polarization and activation, we are interested in combining the whole cell modeling framework for intracellular calcium dynamics involving Mitochondria and Endoplasmic Reticulum relocation with a stochastic model for calcium release activated channel (CRAC) assembly on the cell membrane via ORAI-STIM interaction. Technically we use the stochastically changing location and capacity of CRACs as point sources for a deterministic reaction-diffusion model for the intracellular calcium dynamics. This hybrid stochastic-deterministic approach will help to understand the complex mechanisms of physiological and pathophysiological characteristics of T-cells, which in turn seek to explain traits of disorders ranging from immunodeficiency to autoimmunity.

P.49 Enhanced adhesion of Streptococcus mutans to hydroxyappatite after exposure to saliva

Christian Spengler[1], Nicolas Thewes[1], Friederike Nolle[1], Thomas Faidt[1], Natalia Umanskaya[2], Matthias Hannig[2], Markus Bischoff[3] and Karin Jacobs[1]

[1]Saarland University, Experimental Physics, 66041 Saarbrücken, Germany,
[2]Clinic of Operative Dentistry, Periodontology and Preventive Dentistry, Saarland University, 66421 Homburg/Saar, Germany and
[3]Institute for Medical Microbiology and Hygiene, Saarland University, 66421 Homburg/Saar, Germany

Streptococcus mutans cells form robust biofilms on human teeth and are strongly related to caries incidents. Hence, understanding the adhesion of *S. mutans* inside the human oral cavity is of major interest for preventive dentistry. We present atomic force microscopy–based single-cell force spectroscopy measurements of *S. mutans* cells on hydroxyapatite, the mineral component of teeth. For comparison, we also use *Staphylococcus carnosus* cells which are non-pathogenic and not related to the oral cavity. We observe for almost all measurements a significant difference in adhesion strength for *S. mutans* as well as for *S. carnosus* cells. However, the increase in adhesion strength after saliva exposure is much higher for S. mutans cells compared to *S. carnosus* cells. Our results demonstrate that S. mutans cells are well adapted to their natural environment, the oral cavity. This ability promotes the biofilm-forming capability of that species and hence the production of caries-provoking acids. In conse-

quence, understanding the fundamentals of this mechanism may pave a way towards more effective caries-reducing techniques [1].

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P.50 Nano-scaled contact area of Staphylococcal cells

Christian Spengler[1], Nicolas Thewes[1], Philipp Jung[2], Markus Bischoff[2] and Karin Jacobs[1]

[1]Saarland University, Experimental Physics, 66041 Saarbrücken, Germany, and [2]Institute for Medical Microbiology and Hygiene, Saarland University, 66421 Homburg/Saar, Germany

Bacterial adhesion is a crucial step during the development of infections as well as the formation of biofilms. Hence, fundamental research of bacterial adhesion mechanisms is of utmost importance. So far, less is known about the size of the contact area between bacterial cells and a surface. This gap is filled by this study using a single-cell force spectroscopy-based method to investigate the contact area between a single S. aureus cell and a solid substrate. The technique relies on the strong influence of the hydrophobic interaction on bacterial adhesion [1]: By incrementally crossing a very sharp hydrophobic/hydrophilic interface while performing force-distance curves with a single bacterial probe, the bacterial contact area can be determined. Assuming circular contact areas, their radii – determined in our experiments – are in the range from tens of nanometers to a few hundred nanometers. The contact area can be slightly enlarged by a larger loading force, yet does not resemble a Hertzian contact, rather, the enlargement is a property of the individual bacterial cell. Additionally, Staphylococcus carnosus has been probed, which is less adherent than S. aureus, yet both bacteria exhibit a similar contact area size. This corroborates the notion that the adhesive strength of bacteria is not a matter of contact area, but rather a matter of which and how many molecules of the bacterial species' cell wall form the contact [2].

[1] N. Thewes *et al.*, Beilstein Journal of Nanotechnology 5, 1501 (2014).
[2] C. Spengler *et al.*, accepted for Nanoscale (2017).

P.51 The role of vimentin in leukocyte amoeboid migration

Luiza Stankevicins[1], Emmanuel Terriac[1], Mira Türknetz[1], Fang Cheng[2], Marta Urbanska[3], John Eriksson[2], Franziska Lautenschläger[1,4].

[1]INM Leibniz Institute for New Materials, Saarbrücken, Germany
[2]Turku Centre for Biotechnology, Turku, Finland
[3]Technische Universität, Dresden, Germany
[4] Faculty of Natural and Technical Sciences- Universität des Saarlandes, Saarbrücken, Germany

Leukocytes use a friction-based migration when moving through the confined interstitial space. The force during movement is generated by dynamic protrusions that create friction with the surrounding extra cellular matrix pushing the cell body forward. Cell migration further implies a continuously cytoskeleton remodeling in order to achieve the shape changes needed to move in between tissues without destroying them. Vimentin is the only cytoplasmic intermediate filament expressed in leukocytes and the most flexible cytoskeletal protein. However, the role of vimentin in leukocyte migration is not well understood. We evaluated the efficiency of migration in leukocytes after vimentin depletion: *in vivo* by primary dendritic cell homing to lymph nodes and *in vitro*, using micro fabricated channels and confining roofs to ensure a microenvironment as close to the natural as possible. For the migration assays we used primary dendritic cells obtained from vimentin wt and ko mice and the cell line HL-60 with the vimentin mutation Y117L, which prevents filaments assembly. In all migration assays, we observed a significant reduced amount of cells able to migrate among vimentin deficient cells. To investigate whether the migration impairment is due to an alteration in the mechanical properties of the cells we measured cell deformation in suspended cells. This was done either in a passive way by subjecting cells to hydrodynamic forces (RTDC methodology, Zellmechanik, Dresden) or in an active way by analysing cell migration in constricted channels. Our results show that vimentin network might regulate cell deformation in coordination with actin filaments. Taken together, these observations suggest that vimentin plays a role in cell deformation and the association between actin and vimentin may have direct implications on cell migration modulation.

P.52 Effect of Different Mouthrinses on Salivary Bacteria *in Vivo*

Nadin Tahan, Natalia Umanskaya, Matthias Hannig

Clinic of Operative Dentistry, Periodontology and Preventive Dentistry, Saarland University, Homburg/ Saar, Germany

Objectives: The aim of this in vivo study was to investigate the antibacterial effect of three different mouthrinses and an oral spray on the salivary flora.
Materials and Methods: Five adult volunteers performed a single wash/ spray of (Chlorhexamed Forte, Biorepair, Elmex Kariesschutz, Theranovis oral spray). Samples of saliva were collected under baseline conditions and at 30 s, 1, 6 and 12 h after performing the tested mouthrinses/ oral spray. The samples were centrifuged, bacterial pellets isolated. The pellets were microscopically examined by BacLight™ viability assay and transmission electron microscopic.
Results: CHX showed high level of antibacterial activity up to six hours. Biorepair and Elmex Kariesschutz have a similar or better immediate antibacterial potential as chlorhexidine, whereas after one hour an obvious recovery in the bacterial vitality was detected. However, Theranovis had the weakest antibacterial action on the salivary flora.
Conclusion: The results of the present study revealed antibacterial effects of all tested mouthrinses/ oral spray on the salivary bacteria. This study allows classification of the tested mouthrinses/ oral spray.

P.53 Cell cortex structure and dynamics before, during and after adhesion

E. Terriac[1] , D. Flormann[1], K. Kaub[1], Z. Mostajeran[1] and F. Lautenschläger[1,2]

[1]Cytoskeletal Fibers, INM Leibniz Institute for New Materials, Saarbrücken, Germany
[2]Faculty of natural and technical Sciences, University of Saarland, Saarbrücken, Germany

Actin filaments are very dynamic protein polymers, able to create super structures within the cell. Among those structures, the actin cortex, which is the actin shell under the membrane, remains not well understood on many aspects. It is mainly composed of actin filaments of different sizes, motor proteins, actin crosslinkers and

membrane linking proteins with a not yet resolved fine structure. The actin cortex is one main component that gives to the cell its elastic properties, crucial for cells to be able to undergo shape changes during tissue formation or migration. A recent study [1] shows some unexpected behavior of the cell mechanics if they are in a suspended state: upon myosin 2 inhibition, the elasticity of adherent cells decreases but, if one is able to perform such experiments on cells without contact to anything, the cells become less compliant. The goal of our project (project A9 in SFB 1027) is to study the changes in the cortex during adhesion in order to understand the different behavior of cell elasticity upon myosin inhibition. This poster is an introduction of the project, describing our workflow for the next years and introducing another poster showing our first results.

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P.54 Photoactivatable Actin Inhibitor Cytochalasin D

Roshna Vakkeel, Shifang Zhao, Emmanuel Terriac, Franziska Lautenschäger, Aránzazu del Campo

INM – Leibniz Institut für Neue Materialien, Saarbrücken, Germany

In cellular shape change, motility and cellular division actin dynamics plays a very crucial role.[1] The assembly of monomeric G-actin into filamentous F-actin into branches leads to cellular shape change via formation of a lamellipodium triggering cell movement. Using actin inhibitors, investigation and regulation of these cellular processes with spatiotemporal regulation of F-actin dynamics can be achieved. Fungal metabolites cytochalasins[2] are effective modulators of actin network organization with good cell permeability and high binding affinity towards the fast growing plus end of the actin microfilaments.[3] Using cytochalsain D, we can spatiotemporally and reversibly disturb the F-actin cytoskeleton and release free actin monomers within the cell. This will allow us to study cytoskeletal dynamics, or how it affects related cellular structures and processes.

Herein, we present photriggerable Cytochalasin D (a potent actin inhibitor) for controlled release to locally disturb F-actin superstructures, like stress fibers, cortical actin networks and finally direct cell motility. The phototriggerable derivative[4] will

also serve as a good method with dosage control of the drug at the required sites of action combined with high bioavailability and subcellular resolution in time scale of minutes.

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P.55 Pattern formation of Min proteins in cellular and open geometries

Lukas Wettmann[1] and Karsten Kruse[2]

[1]*Theoretische Physik, Universität des Saarlandes, Postfach 151150, 66041 Saarbrücken, Germany*

[2]*NCCR Chemical Biology, Departments of Biochemistry and Theoretical Physics, University of Geneva, 1211 Geneva, Switzerland*

The site of cell division in *Escherichia coli* bacteria is determined through the self-organization of the Min proteins. They exert pole-to-pole oscillations in wild-type cells but several other patterns have been found *in vivo* and by *in vitro* reconstitution. We use a model based on transient binding of MinE to the cytoplasmic membrane to analyze the dynamics of the Min proteins in dierent cell geometries, including basic geometric shapes and rectangles of varying length/width ratios. For open geometries, we are able to reproduce the observed spiral patterns and travelling waves.

P.56 Detecting regulatory protein complexes that define pluripotency

T. Will[1,2] and V. Helms[1]

[1]Center for Bioinformatics, and 2Graduate School of Computer Science, Saarland University, Saarbrücken, Germany

Eukaryotic gene expression is controlled by molecular logic circuits that integrate regulatory signals of many different factors. In particular, complexation of transcription factors (TFs) and other regulatory proteins is a prevailing and evolutionary conserved mechanism of signal integration within critical regulatory pathways. Knowledge on the assembly of such complexes can enable us to infer the target genes that are cooperatively controlled as well as the exerted regulatory mechanisms of all proteins involved, including potentially recruited coregulators.

We demonstrated for TF complexes in yeast that combining protein interaction data with domain–domain interaction data by our algorithm DACO yields superior predictions of the combinatorial manifold of TF complexes compared to existing methods that are designed to detect self-contained functional modules. Furthermore, we were able to assign many of the predictions to target genes as well as to a potential regulatory effect in agreement with literature evidence. Currently we are upscaling and expanding the capabilities of our software tools. To generate sample-specific interactome data as the input for DACO, for example, we subsequently developed the tool PPIXpress that exploits expression data at the transcript-level and is able to construct contextualized protein and domain interaction networks with isoform-resolution that even account for the effects of alternative splicing.

By inferring such specific interactomes for public data on human embryonic stem and iPS cells as well as other samples of the ENCODE and ROADMAP projects, we could predict the TF complexomes found in those cell states. Our most recent developments finally allow quantifying the abundance of the complexes per sample and enabled us to pin down a set of differential TF complexes of significantly higher abundance in pluripotent cells. Those particular complexes contain many known drivers of pluripotency and allowed us to construct a gene regulatory network of pluripotency that even considers cooperativity between proteins.

P.57 Cancer Progression Alters Morphological Fluctuation and Migration of Human Gastric Cells

Akihisa Yamamoto[1,2], Yusuke Sakamaki[2], Tatsuaki Tsuruyama[1], and Motomu Tanaka[2,3]

[1]Graduate school of Medicine, 2Institute for Integral Cell-Material Sciences, Kyoto University, Kyoto, Japan
[3]Physical Chemistry of Biosystems, University of Heidelberg, Heidelberg, Germany

The structure of multicellular tissues becomes disordered according to the cancer progression, and single cells display a wider variety in size and shape (pleomorphism). Although this static, phenomenological information is utilized as an indicator of cancer staging in the field of pathology, little is known about the mechanism on how the collective ordering in tissues and the dynamics of single cells are correlated during the cancer progression. In this research, we describe human gastric cells at different cancer stages as self-propelled deformable particles [1], and aim to reveal the correlation between their adhesion, active deformation, and migratory motion.
To model the interactions between gastric cells and extracellular environments, we functionalized the surface of supported membranes [2] with laminin, which is the main component of basal lamina [3]. Active deformation of the adhesion zone of human gastric cells in four different cancer stages was recorded with a label-free, reflection interference contrast microscopy (RICM). We found that well differentiated "healthy" cancer cells hardly migrate nor deform, while poorly differentiated "sick" cancer cells actively deform and migrate. Our data unraveled that active shape fluctuation and migration are clearly correlated with cancer progression.

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P.58 Evaluating the protective properties of plant extracts by analyzing the *in-situ* initial biofilm

Nazife Yazdani [1], Simone Trautmann [1], Claudia Fecher-Trost [2], Matthias Hannig [1]

[1] *Clinic for Operative Dentistry , Periodontology and Preventive Dentistry, University of the Saarland, Homburg, Germany*

[2] *Experimental and Clinical Pharmacology and Toxicology, University of the Saarland, Homburg, Germany*

Dental erosion is the loss of tooth structure caused by acidic impact. Its prevalence is still increasing. The initial biofilm - resulting from the selective adsorption of salivary proteins to the enamel - plays a big role to protect the tooth. Plant extracts as rinsing solutions are a possible approach to improve protective properties of the biofilm.
Changes of biofilm proteome after rinsing with different plant extracts were analyzed quantitatively and qualitatively by mass spectrometry (nano-LC-MS/MS). Also, to investigate the influence of these plant extracts on the protective property of the biofilm against erosive mineral loss and their action as an ion reservoir inside the modified biofilm, ultrastructure and acid resistance of the biofilm were evaluated by transmission electron microscopy (TEM). The release of calcium- and phosphate ions was measured photometrically.
Different protein distribution patterns with more than 250 proteins were identified. Under the influence of the tested plant extracts, a lower amount of protein species could be identified compared to the control. In contrast, the biofilm density was increased and the modified initial biofilm was of higher tenacity than the control in an acidic milieu. Calcium- and phosphate measurements showed higher levels of ions release suggesting the biofilm treated with plant extracts as a potential ion reservoir.

P.59 A platform to study the role of forces in T lymphocyte activation

J Zhang [1,2], B Qu[3], M Hoth[3], A del Campo [1,2]

[1]*INM Leibniz Institute for New Materials, Saarbrücken, Germany*
[2]*Chemistry Department, Saarland University, Germany*
[3]*Center for Integrative Physiology and Molecular Medicine (CIPMM), Saarland University, Germany*

T cell activation requires the recognition by T-cell receptors (TCR) of peptide-major histocompatibility complex molecules (pMHC) presented by antigen-presenting cells (APC). This process also involves engagement of costimulatory receptors, cytoskeletal components and adhesion molecules recognizing ligands on APC, finally forming a special cell-cell structure-immunological synapse (IS) [1].
Although the biochemical and molecular aspects of this cell-cell interaction have been well studied, the possible role of mechanical forces in receptor assembly at the IS and T cell activation has only recently been investigated. Experimental evidence shows that the T cell surface is subjected to tensile and traction forces which could be transmitted to TCR-pMHC or other receptor pairs [2]. T cells could also use forces to sense the physical properties of the APC to translate them into biochemical signals. In current models of APC-T cell interactions, the mechanical engagement of costimulatory receptors and adhesion molecules have rarely been considered. So in our project, we will use hydrogel to fabricate artificial APCs recapitulate both mechanical and biochemical information which could be recognized by T cells, to study how mechanical engagement of individual receptors correlates with activation levels in T cells.

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P.60 The role of TMX oxidoreductases in melanoma growth and invasion

Xin Zhang, Adina Monica Vultur and Ivan Bogeski

Institut für Herz- und Kreislaufphysiologie, Universitätsmedizin Göttingen, Göttingen, Germany

Calcium and redox signals are essential regulators of melanoma pathobiology[1]. However, information regarding molecular players involved is scarce. Here we examined the role of endoplasmic reticulum (ER)-based protein disulfide isomerases (PDI) family members thioredoxin-related transmembrane proteins 1 and 3 (TMX1, TMX3) in melanoma. Our results show that TMX1 and TMX3 are upregulated in human melanoma samples. TMX1 downregulation inhibited melanoma cell proliferation and migration in vitro and tumor growth in vivo. Moreover, TMX1-silencing led to inhibition of NFAT1 nuclear translocation, a transcription factor present in melanoma but absent in healthy melanocytes. TMX1-silenced melanoma cells displayed an enhanced mitochondrial calcium uptake and subsequent increase in intracellular H2O2 levels which were responsible for NFAT1 inhibition via oxidation of calcineurin. Antioxidant treatment reversed the TMX1-induced NFAT1 inhibition. Electron microscopy of TMX1-silenced cells depicted an altered mitochondrial morphology and distances between mitochondria and ER and plasma membrane and thereby provided evidence regarding the molecular mechanism leading to TMX1-induced inhibition of NFAT1 activity and thus melanoma growth and invasion. In summary, our study identified a novel TMX1-NFAT1 signaling axis that regulates melanoma pathobiology in a calcium and redox dependent manner. TMX1 and NFAT1 represent potential novel therapeutic targets as well as biomarkers of aggressive melanoma disease.

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P.61 Light-driven force application on individual cell-ECM contacts

Yijun Zheng [1], Aleeza Farrukh[1], Arzu Colak[1], Jean-Rémy Colard-Itté[3], Damien Dattler[3], Nicolas Giuseppone[3,4], Andres Garcia[5,6], Roland Bennewitz[1], Aránzazu del Campo[1,2]

[1]INM Leibniz Institute for New Materials, Campus D22, 66123, Saarbrücken, Germany
[2]Chemistry Department, Saarland University, 66123, Germany
[3]SAMS research group, Institut Charles Sadron, University of Strasbourg – CNRS, 23 rue du Loess, BP 84047, 67034 Strasbourg Cedex 2, France
[4]Institut Charles Sadron, University of Strasbourg – CNRS, 23 rue du Loess, BP 84047, 67034 Strasbourg Cedex 2, France.
[5]Woodruff School of Mechanical Engineering, Georgia Institute of Technology, Atlanta, Georgia 30332, USA
[6]Petit Institute for Bioengineering and Bioscience, Georgia Institute of Technology, Atlanta, Georgia 30332, USA

Mechanical force is one of the most important factors that guide cell's behavior. Several approaches, including micropipettes and single-molecule techniques, magnetic actuation of nanoparticles and micropillars etc, have been developed to apply spatially confined mechanical inputs to cell. These methods, however, could be difficult to manipulate forces with molecular specificity and high spatiotemporal resolution. Photoswitches and optogenetic constructs are sharpening lengths- and timescales for activation and observation of biological phenomena. However, it is still challenging to develop molecular systems that can transfer light into mechanical force in a well-predictable way.

We present a novel approach for applying forces to cells with molecular specificity and at molecular resolution using a light-driven synthetic molecular motor. The motor is modified with two orthogonal sets of polymer chains in its upper and bottom parts. It is immobilized on a biomaterial and contains adhesive ligands at two free ends. Upon light exposure, the molecular motor rotates and twists the entangled polymer chains, thereby applying a mechanical load to receptor-ligand complexes on cell surface. Optomechanical actuation at cell-biomaterial contacts and its consequences will be demonstrated.

P.62 Modeling of auxin membrane transport and accumulation: implication for study of root growth inhibition by auxin

Maria Akhmanova, Matyáš Fendrych

IST Austria, Klosterneuburg, Austria

Plant roots have an outstanding ability to grow in the direction of gravity or nutrients [1]. Bending of the root tip in the preferred direction is achieved by asymmetric cell growth on the opposite sides of the root, dictated by asymmetrical distribution of the hormone auxin, which inhibits cell elongation in a concentration dependent manner. However, mechanism of growth inhibition remains unclear. To study this phenomenon, the knowledge of auxin concentration inside the cells is essential, which is difficult to measure. By contrast, auxin membrane transport is well characterized: auxin is pumped by carrier proteins in and out of the cells [2]. Computational models can help to integrate available data on transporters to predict spacial and temporal dynamics of auxin.

We constructed a 2D-axisymmetrical finite-element model of the root using COMSOL Multiphysics software. Model geometry comprises individual cells, separated by extracellular space, and an outer domain to account for auxin concentration in the media. Membrane permeability for auxin is assigned for each boundary depending on carrier localization. Auxin accumulation ratio shows highest concentration in the outer cell layer and a gradient along the root. Using the model we analyze the growth rates after auxin application and find time delay between computed auxin accumulation and growth inhibition.

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P.63 Spontaneous contraction of poroelastic actomyosin sheets

Jonathan Salmerón[1], Anne Bernheim-Groswasser[2], Karsten Kruse[1]

[1]*Theoretical Physics Applied to Biology and Biochemistry Departments, University of Geneva, Switzerland*
[2]*Department of Chemical Engineering, Ben Gurion, University of the Negev, Israel*

Reconstituted systems play an important role for understanding cytoskeletal self-organisation. Motivated by experiments in the group of Anne Bernheim, Ben Gurion University, Israel, we study theoretically the contraction of an actin gel. In the experiments a strong outward flux of buffer is observed. In addition, the gel spontaneously buckles. We use a hydrodynamic approach to study this dynamics. In this description, we consider two components, an active elastic component and a viscous passive component that describe the actomyosin network and the buffer, respectively. The solutions to our equations show that contraction is initiated at the gel boundary and that the outward velocity of the solvent can exceed the gel contraction velocity if the gel volume fraction is larger than the solvent volume fraction.

List of Partcipants

Ahkmanova, Maria	IST Austria, Klosterneuburg, Austria *maria.akhmanova@ist.ac.at*
Alert, Ricard	University of Barcelona, Barcelona, Spain *ricard.alert@fmc.ub.edu*
Arita, Chikashi	Saarland University, Saarbrücken, Germany *chikashi.arita@lusi.uni-sb.de*
Arroyo, Marino	Universitat Politècnica de Catalunya, Barcelona, Spain *marino.arroyo@upc.edu*
Bahr, Daniel	Saarland University, Saarbrücken, Germany *bahr@lusi.uni-sb.de*
Barberi, Luca	LPTMS, Univ. Paris-Sud, Orsay, France *luca.barberi@u-psud.fr*
Bashar, Reda	Saarland University, Homburg, Germany *Bashar.Reda@uks.eu*
Basu, Saikat	Indian Association for the Cultivation of Science, Kolkata, India *sspsb2@iacs.res.in*
Becker, Björn	Saarland University, Saarbrücken, Germany *bjoern_becker2@gmx.de*
Bennett, Robert	University of Freiburg, Freiburg, Germany *robert.bennett@physik.uni-freiburg.de*
Blanch-Mercader, Carles	University of Geneva, Geneva, Switzerland *Carles.BlanchMercader@unige.ch*
Böckmann, Rainer	University of Erlangen-Nürnberg, Erlangen, Germany *rainer.boeckmann@fau.de*
Bogeski, Ivan	University of Göttingen, Göttingen, Germany *ivanbogeski@yahoo.com*
Bonn, Daniel	University of Amsterdam, Amsterdam, Netherlands *d.bonn@uva.nl*
Bozem, Monika	Saarland University, Homburg, Germany *monika.bozem@uks.eu*
Brugues, Jan	Max Planck Institute for Molecular Cell Biology and Genetics, Dresden, Germany *brugues@mpi-cbg.de*

Bruns, Dieter	Saarland University, Homburg, Germany *dieter.bruns@uks.eu*
Casademunt, Jaume	Universitat de Barcelona, Barcelona, Spain *jaume.casademunt@ub.edu*
Chan, Chii	EMBL Heidelberg, Heidelberg, Germany *cchan@embl.de*
Cingolani, Lorenzo	Italian Institute for Technology, Genova, Italy *lorenzo.cingolani@iit.it*
Cohen, Ohad	Weizmann Institute of Science, Rehovot, Israel *ohad.cohen@weizmann.ac.il*
Dahmke, Indra Navina	INM Leibniz Institute for New Materials, Saarbrücken, Germany *indra.dahmke@leibniz-inm.de*
Davoudi, Neda	University of Kaiserslautern, Kaiserslautern, Germany *davoudi@physik.uni-kl.de*
de Jonge, Niels	INM Leibniz Institute for New Materials, Saarbrücken, Germany *Niels.deJonge@leibniz-inm.de*
del Campo, Aránzazu	INM Leibniz Institute for New Materials, Saarbrücken, Germany *aranzazu.delcampo@leibniz-inm.de*
Deviri, Dan	Weizmann institute of science, Rehovot, Israel *dan.deviri@weizmann.ac.il*
Dhara, Madhurima	Saarland University, Homburg, Germany *madhurimadhara@gmail.com*
Dubey, Sushil	Condensed Matter Group, Raman Research institute, Bangalore, India *dubeys@rri.res.in*
Dudek, Johanna	Saarland University, Homburg, Germany *johanna.dudek@uks.eu*
Dufrêne, Yves	University of Leuven, Leuven, Belgium *yves.dufrene@uclouvain.be*
Ecker, Nicolas	University of Geneva, Geneva, Switzerland *nicolas.ecker@unige.ch*
Eisenbeis, Janina	Saarland University, Homburg, Germany *janina.eisenbeis@uks.eu*

Ettrich, Rudi	Center f. Nanobiol. & Structural Biol., Nove Hrady, Czechia *ettrich@nh.cas.cz*
Fabry, Ben	University of Erlangen-Nürnberg, Erlangen, Germany *bfabry@biomed.uni-erlangen.de*
Faidt, Thomas	Saarland University, Saarbrücken, Germany *t.faidt@physik.uni-saarland.de*
Faure, Laura	Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain *faure.laura.marie@gmail.com*
Fedosov, Dmitry	FZ Jülich, Jülich, Germany *d.fedosov@fz-juelich.de*
Finkler, Marc	Saarland University, Saarbrücken, Germany *Marc.Finkler@uni-saarland.de*
Fleury, Jean-Babtiste	Saarland University, Saarbrücken, Germany *jean-baptiste.fleury@physik.uni-saarland.de*
Flormann, Daniel	Saarland University, Saarbrücken, Germany *Daniel.Flormann@web.de*
Fredrich, Thierry	Saarland University, Saarbrücken, Germany *thierry@lusi.uni-sb.de*
Fries, Peter	Saarland University, Saarbrücken, Germany *s9prfrie@stud.uni-saarland.de*
Gahbauer, Stefan	University of Erlangen-Nürnberg, Erlangen, Germany *stefan.gahbauer@fau.de*
Garcia Manyes, Sergi	Kings College, London, UK *sergi.garcia-manyes@kcl.ac.uk*
Giri, Varun	Saarland University, Saarbrücken, Germany *v.giri@physik.uni-saarland.de*
Glitsch, Maike	University of Oxford, Oxford, UK *maike.glitsch@dpag.ox.ac.uk*
Gómez-González, Manuel	Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain *mgomez@ibecbarcelona.eu*
Griffo, Alessandra	Aalto University, Espoo, Finland *alessandra.griffo@aalto.fi*
Grosse, Petra	Journal of Cell Science, Cambridge, UK *petra.gross@biologists.com*

Grosse, Robert	Biochemical-Pharmacological Center Marburg, Marburg, Germany *robert.grosse@staff.uni-marburg.de*
Guck, Jochen	Technical University Dresden, Dresden, Germany *jochen.guck@tu-dresden.de*
Hadjivasiliou, Zena	University of Geneva, Geneva, Switzerland *zena.hadjivasiliou@unige.ch*
Hafner, Anne	Saarland University, Saarbrücken, Germany *anne.hafner@lusi.uni-sb.de*
Hähl, Hendrik	Saarland University, Saarbrücken, Germany *h.haehl@physik.uni-saarland.de*
Han, Mitchell	INM Leibniz Institute for New Materials, Saarbrücken, Germany *Mitchell.Han@leibniz-inm.de*
Hannig, Matthias	Saarland University, Homburg, Germany *matthias.hannig@uks.eu*
Harb, Ali	Saarland University, Homburg, Germany *ali.harb@uks.eu*
Helms, Volkhard	Saarland University, Saarbrücken, Germany *volkhard.helms@bioinformatik.uni-saarland.de*
Hillringhaus, Sebastian	FZ Jülich, Jülich, Germany *s.hillringhaus@fz-juelich.de*
Hofherr, Linda	University of Kaiserslautern, Kaiserslautern, Germany *lhofherr@physik.uni-kl.de*
Holz, Danielle	Lehigh University, Bethlehem (PA), USA *dah414@Lehigh.edu*
Horan, Brandon	Lehigh University, Bethlehem (PA), USA *bgh314@lehigh.edu*
Hornak, Ivan	Saarland University, Saarbrücken, Germany *hornak@lusi.uni-sb.de*
Hui, Xin	Saarland University, Homburg, Germany *xin.hui@uks.eu*
Huttenlochner, Katharina	University of Kaiserslautern, Kaiserslautern, Germany *huttenlochner@physik.uni-kl.de*
Iturri, Jagoba	BOKU University for Natural Resources and Life Sciences, Vienna, Austria *jagoba.iturri@boku.ac.at*

Jacobs, Karin	Saarland University, Saarbrücken, Germany *k.jacobs at physik.uni-saarland.de*
Jagoba, Iturri	BOKU University for Natural Resources and Life Sciences, Vienna, Austria *jagoba.iturri@boku.ac.at*
Jiang, Qiyang	INM Leibniz Institute for New Materials, Saarbrücken, Germany *Qiyang.Jiang@leibniz-inm.de*
Jose, Robin	Saarland University, Saarbrücken, Germany *rjose@lusi.uni-sb.de*
Joseph, Desna	INM Leibniz Institute for New Materials, Saarbrücken, Germany *desna.joseph@leibniz-inm.de*
Jung, Philipp	Saarland University, Homburg, Germany *philipp.jung@uks.eu*
Kale, Sohan	Universitat Politècnica de Catalunya, Barcelona, Spain *sohan.sudhir.kale@up.edu*
Kasper, Jennifer	INM Leibniz Institute for New Materials, Saarbrücken, Germany *jennifer.kasper@leibniz-inm.de*
Kaub, Kevin	Saarland University, Saarbrücken, Germany *s9kekaub@stud.uni-saarland.de*
Kechagia, Jenny Zanetta	IBEC, Barcelona, Spain *jkechagia@ibecbarcelona.eu*
Keller, Fabian	Westfälische Wilhelms-Universität, Münster, Germany *fabiankeller@wwu.de*
Khan, Essak	INM Leibniz Institute for New Materials, Saarbrücken, Germany *essak.khan@leibniz-inm.de*
Kierfeld, Jan	TU Dortmund University, Dortmund, Germany *jan.kierfeld@tu-dortmund.de*
Kirsch, Sonja	University of Erlangen-Nürnberg, Erlangen, Germany *sonja.kirsch@fau.de*
Klughammer, Nils	Heidelberg University, Heidelberg, Germany *nils.klughammer@bioquant.uni-heidelberg.de*
Knapp, Phillip	Saarland University, Saarbrücken, Germany *phillip.knapp@uni-saarland.de*

Kondev, Jane	Brandeis University, Waltham (MA), USA *Kondev@brandeis.edu*
Köster, Sarah	University of Göttingen, Göttingen, Germany *sarah.koester@phys.uni-goettingen.de*
Kruse, Karsten	University of Geneva, Geneva, Switzerland *karsten.kruse@unige.ch*
Kunnas, Peter	INM Leibniz Institute for New Materials, Saarbrücken, Germany *peter.kunnas@leibniz-inm.de*
La Porta, Caterina	University of Milan, Milan, Italy *Caterina.laporta@unimi.it*
Lemke, Lilia	Clinic of operative Dentistry, Periodontology and Preventive Dentistry, Homburg, Germany *lilia.lemke@uks.eu*
Li, Menglin	Saarland University, Saarbrücken, Germany *leonard.li@physik.uni-saarland.de*
Li, Bin	INM Leibniz Institute for New Materials, Saarbrücken, Germany *in.Li@leibniz-inm.de*
MacKintosh, Frederick	Rice University, Houston (TX), USA *fcmack@gmail.com*
Maier, Berenike	University of Cologne, Köln, Germany *berenike.maier@uni-koeln.de*
Maikranz, Erik	Saarland University, Saarbrücken, Germany *erik@lusi.uni-sb.de*
Milotti, Edoardo	University of Trieste, Trieste, Italy *milotti@units.it*
Mischo, Johannes	Saarland University, Saarbrücken, Germany *j.mischo@physik.uni-saarland.de*
Mohammadi-Kambs, Mina	Saarland University, Saarbrücken, Germany *m.mohammadi@physik.uni-saarland.de*
Mohrmann, Ralf	Saarland University, Homburg, Germany *ralf.mohrmann@uks.eu*
Monzon, Gina	Saarland University, Saarbrücken, Germany *g.monzon@lusi.uni-sb.de*
Mostajeran, Zahra	Saarland University, Saarbrücken, Germany *zahra.mostajeran@leibniz-inm.de*

Müller, Frank	Saarland University, Saarbrücken, Germany *f.mueller@mx.uni-saarland.de*
Nandi, Saroj	Weizmann Institute of Science, Rehovot, Israel *sarojnandi@gmail.com*
Nasedkin, Alexandr	University of Technology, Gothenburg, Sweden *alexandr.nasedkin@chalmers.se*
Nazarieh, Maryam	Saarland University, Saarbrücken, Germany *maryam.nazarieh@bioinformatik.uni-saarland.de*
Nedelec, Francois	EMBL Heidelberg, Heidelberg, Germany *nedelec@embl.de*
Niemeyer, Barbara A.	Saarland University, Homburg, Germany *barbara.niemeyer@uks.eu*
Nobre, Cíntia	Saarland University, Homburg, Germany *cintia_nobre@hotmail.com*
Nolle, Friederike	Saarland University, Saarbrücken, Germany *f.nolle@physik.uni-saarland.de*
Olsen, Lars Folke	University of Southern Denmark, Odense, Denmark *lfo@bmb.sdu.dk*
Oriola, David	Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany *oriola@mpi-cbg.de*
Palty, Raz	Technion, Haifa, Israel *razpalty@technion.ac.il*
Peckys, Diana B.	Saarland University, Homburg, Germany *diana.peckys@uks.eu*
Plessner, Matthias	Philipps University, Marburg, Germany *matthias.plessner@uni-marburg.de*
Ramesh, Girish	Saarland University, Homburg, Germany *girish.ramesh@uks.eu*
Reda, Bashar	Saarland University, Homburg, Germany *Bashar.Reda@uks.eu*
Renping, Zhao	Saarland University, Homburg, Germany *renping.zhao@gmail.com*
Rieger, Heiko	Saarland University, Saarbrücken, Germany *h.rieger@mx.uni-saarland.de*

Ritort, Felix	University of Barcelona, Barcelona, Spain *ritort@ub.edu*
Roca-Cusachs, Pere	Institute für Bioengineering of Catalonia, Barcelona, Spain *rocacusachs@ub.edu*
Sadjadi, Zeinab	Helmholtz Center for Infection research, Department of System Immunology, Braunschweig, Germany *zeinabsadjadi@gmail.com*
Saggiorato, Guglielmo	LPTMS, Univ. Paris-Sud, Orsay, France *guglielmo.saggiorato@lptms.u-psud.fr*
Salmerón Hernández, Jonathan	University of Geneva, Geneva, Switzerland *jonathan.salmeron@etu.unige.ch*
Sankaran, Shrikrishnan	INM Leibniz Institute for New Materials, Saarbrücken, Germany *shrikrishnan.sankaran@leibniz-inm.de*
Santen, Ludger	Saarland University, Saarbrücken, Germany *santen@lusi.uni-sb.de*
Schmidt, Barbara	Saarland University, Saarbrücken, Germany *ba.schmidt@gmx.net*
Schmitt, Manfred	Saarland University, Saarbrücken, Germany *mjs@microbiol.uni-sb.de*
Schoppmeyer, Rouven	Saarland University, Homburg, Germany *r.schoppmeyer@gmail.com*
Schwarz, Ulrich	Heidelberg University, Heidelberg, Germany *schwarz@thphys.uni-heidelberg.de*
Shaebani, Reza	Saarland University, Saarbrücken, Germany *shaebani@lusi.uni-sb.de*
Shamipour, Shayan	IST Austria, Klosterneuburg, Austria *sshamip@ist.ac.at*
Sokolowski, Thomas R.	IST Austria, Klosterneuburg, Austria *tsokolowski@ist.ac.at*
Soni, Bhavesh	Saarland University, Saarbrücken, Germany *bsoni@lusi.uni-sb.de*
Spengler, Christian	Saarland University, Saarbrücken, Germany *c.spengler@physik.uni-saarland.de*
Stankevicins, Luiza	INM Leibniz Institute for New Materials, Saarbrücken, Germany *luiza.stankevicins@leibniz-inm.de*

Tahan, Nadin	Saarland University, Homburg, Germany *Nadin.Tahan@uks.eu*
Terriac, Emmanuel	INM Leibniz Institute for New Materials, Saarbrücken, Germany *emmanuel.terriac@leibniz-inm.de*
Tkacik, Gasper	IST Austria, Klosterneuburg, Austria *gtkacik@ist.ac.at*
Trautmann, Simone	Saarland University, Homburg, Germany *simone.trautmann@uks.eu*
Trepat, Yavier	Inst. f. Bioengineering of Catalonia, Barcelona, Spain *xtrepat@ibecbarcelona.eu*
Vakkeel, Roshna	INM Leibniz Institute for New Materials, Saarbrücken, Germany *Roshna.Vakkeel@leibniz-inm.de*
Vesperini, Doriane	UTC - BMBI, Compiègne, France *doriane.vesperini@utc.fr*
Wasnik, Vaibhav	University of Geneva, Geneva, Switzerland *wasnik.vaibhav@gmail.com*
Wettmann, Lukas	Saarland University, Saarbrücken, Germany *lwettmann@gmx.de*
Will, Thorsten	Saarland University, Saarbrücken, Germany *thorsten.will@bioinformatik.uni-saarland.de*
Wolf, Katarina	Radboud University Medical Centre, Nijmegen, Netherlands *katarina.wolf@radboudumc.nl*
Wysocki, Adam	Saarland University, Saarbrücken, Germany *a.wysocki@lusi.uni-sb.de*
Xiang, Shengnan	University of Freiburg, Freiburg, Germany *xsn20005@163.com*
Yamamoto, Akihisa	Kyoto University, Kyoto, Japan *ayamamoto@icems.kyoto-u.ac.jp*
Yazdani, Nazife	Saarland University, Homburg, Germany *nazife.yazdani@uks.eu*
Yong, Liu	Saarland University, Homburg, Germany *yongliu101510@gmail.com*
Zahra, Hemmati Fard	Saarland University, Saarbrücken, Germany *s8zahemm@stud.uni-saarland.de*

Zaidel-Bar, Ronen	Tel-Aviv University, Tel-Aviv, Israel *zaidelbar@gmail.com*
Zapperi, Stefano	University of Milan, Milan, Italy *Stefano.zapperi@unimi.it*
Zayer, Rhaleb	Max Planck Institute for Informatics, Saarbrücken, Germany *rzayer@mpi-inf.mpg.de*
Zhang, Jingnan	INM Leibniz Institute for New Materials, Saarbrücken, Germany *Jingnan.Zhang@leibniz-inm.de*
Zhang, Xin	University of Göttingen, Göttingen, Germany *zhangxin02st@gmail.com*
Zheng, Yijun	INM Leibniz Institute for New Materials, Saarbrücken, Germany *Yijun.Zheng@leibniz-inm.de*
Zieske, Katja	UCSF, San Francisco, USA *katja.zieske@ucsf.edu*

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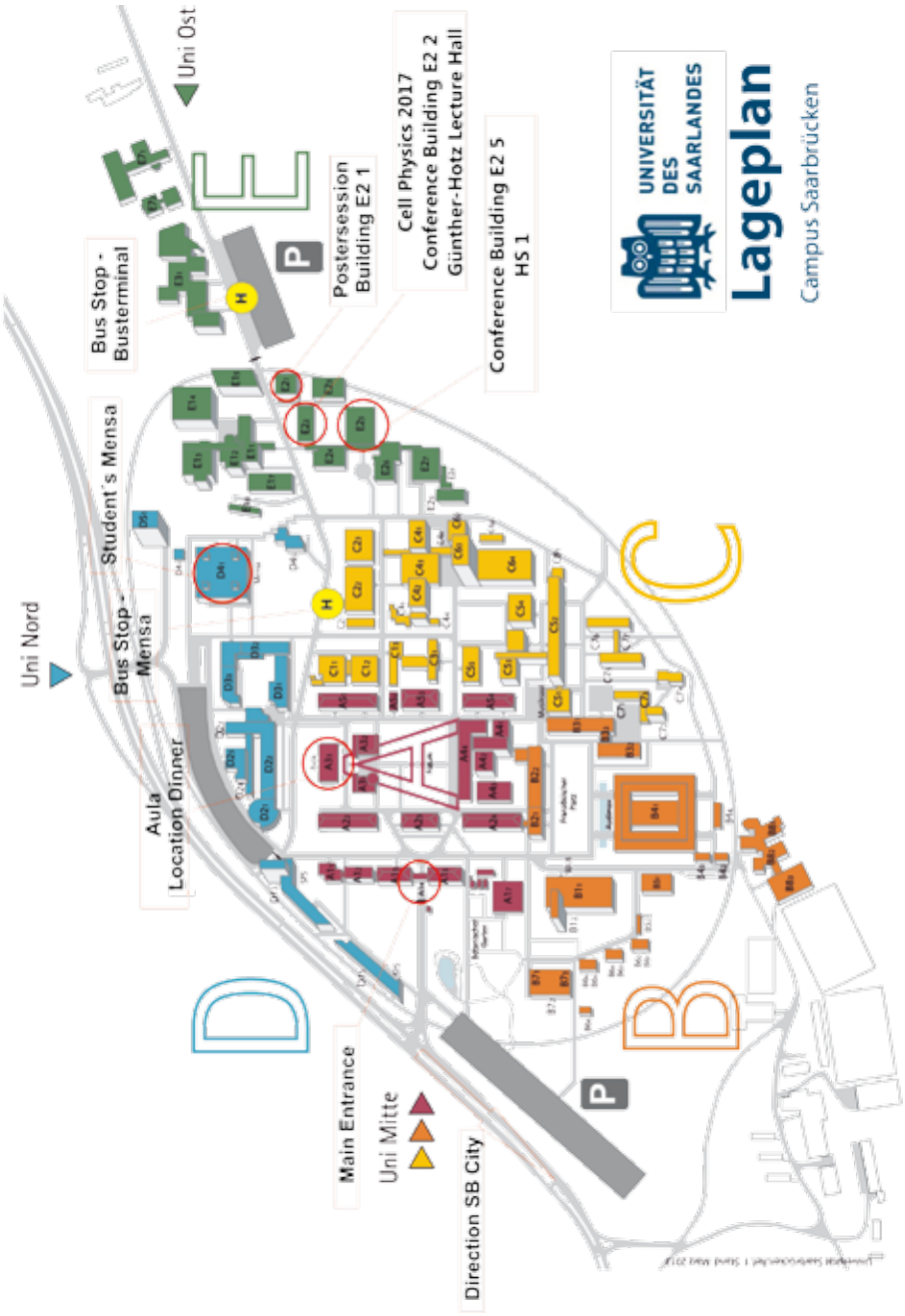
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	WEDNESDAY (11.10.)		THURSDAYDAY (12.10.)		FRIDAY (13.10.)	
8:45-9:00	Opening					
9:00-10:30	**Cytoskeleton I** (30 min. each) • Fabry • Köster • Arroyo		**Cell Mechanics I** (30 min. each) • Guck • Dufrene • Jacobs (15 min.) • Maier		**Cell Mechanics II** (30 min. each) • Schwarz • Trepat • La Porta / Zapperi (45 min.)	
	Coffee					
11:00-12:30	**Orai / Calcium** (30 min. each) • Palty • Ettrich • Glitsch		**Nucleus** (30 min. each) • Kondev • Wolf • Roca-Cusachs		**Adhesion** (15 min. each) • Hofherr • Huttenlochner • Iturri • Akhmanova	**Cancer/films** (15 min. each) • Milotti • Xiang • Saggiorato • Vesperini • Liu
12:30-14:00	Lunch					
14:00-15:30	**Active Matter** (30 min. each) • MacKintosh • Ritort • Bonn		**Cytoskeleton II** (30 min. each) • Nedelec • Grosse • Zaidel-Bar		**Proteins/Genes** (30 min. each) • Garcia Manyes • Cingolani • Tkacik	
15:30-16:00	Coffee				CLOSING (5 min) / Poster Awards	
16:00-17:30	**Cell Mechanics I** (15 min. each) • Casademunt • Blanch-Mercader • Holz • Alert • Hillringhaus Chan	**Cytoskeleton** (15 min. each) • Kierfeld • Brugues • Nasedkin • Dubey • Horan • Hafner	**Cell Mechanics II** (15 min. each) • Fedosov • Cohen • Deviri • Klughammer • Sankaran • Shamipour	**Proteins / Genes** (15 min. each) • Nandi • Dahmke • De Jonge • Gahbauer • Vaibhav • Sokolowski		
17:30-19:00	Poster I		Poster II			
19:00	Dinner					