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 Recent unpublished observations by our collaborators from the Roux Lab in Geneva have shown how the addition of two further ESCRT-III subunits, namely Vps2 and Vps24, can make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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[3] P.D. Bieniasz, Virology, 344(1):55-63 (2006)
[4] N. Chiaruttini et al., Cell, 163(4):866-79 (2015)
[5] M. Lenz *et al*., Phys. Rev. Lett., 103(3):038101 (2009)

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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[2] B. Becker, A. Blum *et al.*, Sci. Rep. (2016).

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]Institute for Physiology, Saarland University, CIPMM, 66424 Homburg/Saar, 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]Leibniz-Institut 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 Pincet[2,4]

[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, Leibniz Institute for New Materials INM, 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]*Leibniz-Institute für neue Materialien, 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 monovalent ions [1]. 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

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, 66123 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, Leibniz Institute for New Materials INM, 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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[2] Chan et al., Biophysical Journal (2015).

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.

[1] D. Hakobyan, A. Heuer, *J. Chem. Phys.* **146**, 064305 (2017)

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-Institut für Neue Materialien,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

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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[3] J. P. Spatz et al., J. Cell Sci. 125, 3765 (2012).

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.

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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.

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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.

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P.41 Calcium-Redox feedback loop in immune cells: New players and regulatory mechanisms (SFB1027 C4)

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 (Hoth & Penner, 1992; Zweifach & Lewis, 1993), 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 (Alansary et al. 2016). 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.

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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 network 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.

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

[1] C. Spengler et al., Journal of Molecular Recognition, 30.7, e2615 (2017).

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].

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[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]Leibniz Institute for New Materials- INM, 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, Leibniz Institute for New Materials INM, 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

Institute of Science and Technology 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.