BP 6: Physics of Cells II

Time: Monday 15:00–17:30 Location: H 1028

Invited Talk BP 6.1 Mon 15:00 H 1028

Intercellular Interactions and the Mystery of Growth Control — •Boris Shraiman — Kavli Institute for Theoretical Physics, UC, Santa Barbara, CA93106, USA

Despite their obvious importance in animal development and disease, the mechanisms that control cell proliferation and tissue growth, are poorly understood. This talk will review the facts, issues and current ideas focusing on the problem of size determination in fly wing development. In particular while proliferation is driven cell autonomously by morphogen growth factors, it appears that the inhibitory control of growth depends on the global tissue-wide profile and history of growth. This global *integration* of growth is likely to be mediated by intercellular interactions involving both mechanics and cell-contact signaling.

BP 6.2 Mon 15:30 H 1028

Optimal cellular mobility for synchronization arising from the gradual recovery of intercellular interactions — •Koichiro Uriu[1], Saul Ares[2], Andrew C. Oates[1], and Luis G. Morelli[1] — [1]Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany — [2]Spanish National Center of Biotechnology CNB-CSIC, Madrid, Spain

Intercellular communication enables the flow of information in living tissues. During embryonic development, tissues undergo massive reorganization involving cellular movements. These cellular movements can be beneficial for the flow of information, because cells get to see effectively more neighbors as they move. However, cells may need some time to establish and develop new communication channels with their new neighbors. Then, if the movement is too fast, they may fail to establish functional communication channels, and movement will be detrimental to information flow. Here we address these questions in the context of moving coupled oscillators, a model system motivated by genetic oscillations in the vertebrate segmentation clock. We find that there is an optimal moving rate for which synchronization is faster and stronger, and a critical moving rate above which synchronization is not possible. These features are the consequence of a competition between the time scale for cellular mobility and that for the recovery of intercellular interaction. Our study indicates that the competition between these two time scales is key to the flow of information in living tissues.

BP 6.3 Mon 15:45 H 1028

The Mechanobiology of *Physarum polycephalum* — •Christina Oettmeier[1,2], Erik Bernitt[1,2], and Hans-Günther Döbereiner[1,2] — [1]Institut für Biophysik, Universität Bremen, 28334 Bremen — [2]Mechanobiology Institute, National University of Singapore, 117411 Singapore

We characterize the mechanobiological properties of *P. polycephalum.* This amoeboid slime mold can reach large sizes and is one single, multinuclear cell. By using microplasmodia, we introduce a reliable and reproducible system for the study of network formation and individual cell motility. Microplasmodia are a special growth form, quasi-spherical in shape and 200-500 microns small. Created by cultivation in shaking culture, they exhibit the same actin-myosin based oscillations as the large plasmodia. We monitor cell dynamics in different ways: First, by observing area oscillations with bright-field microscopy, whereby the spatio-temporal dynamics of focal area and contour could be analyzed. Fast oscillations with a period of 1-2 min as well as a superimposed slow oscillation with a period of about 20 min were found. The second method, calcium imaging with the ratiometric dye Fura-2-AM, was used to clarify the correlation between biochemical signalling and contractions. These correlate with a low local calcium concentration, corresponding to *Physarum*'s calcium-inhibited actin-myosin interaction. Third, the viscoelastic properties were investigated using a microindentation setup. In conclusion, we have shown that microplasmodia are very well suited to study the mechanobiology of *Physarum* due to the reliability, robustness and precision of the system.

BP 6.4 Mon 16:00 H 1028

Mutant cell dynamics in hierarchical organized tissues and resistance development to molecular targeted treatment strategies — •Benjamin Werner and Arne Traulsen — Max Planck Institut für Evolutionsbiologie, Plön, Germany

Most cancers are caused by either a single or more often an accumulation of mutations and thereby altered cell differentiation properties. Nowadays many of these mutations are known and in individual cases molecular targeted drugs were developed, converting ultimate life threatening into chronic diseases. Unfortunately cancer cells tend to develop resistance, leading to treatment failures. We analyze a resistance inducing experiment by applying a minimalistic mathematical model and are able to infer important system parameters, highlighting different resistance mechanism [1]. Translating these in vitro results into an in vivo dynamics is challenging, due to complex cell interactions in hierarchical organized tissues. A minimalistic individual based mathematical model allows us to describe basic properties of mutant cell dynamics in such tissues, most important the cell compartment of the mutant origin and the time development of the mutant population [2]. From this it is apparent that small differences in vitro can lead to important consequences in vivo.

[1] Werner B, Lutz D, Brümmendorf TH,Traulsen A, Balabanov S (2011) Dynamics of resistance development to imatinib. PLoS One .

[2] Werner B, Dingli D, Lenaerts T, Pacheco J, Traulsen A (2011) Dynamics of mutant cells in hierarchical organized tissues. PLoS Comput Biol .

BP 6.5 Mon 16:15 H 1028

Mechanical response of living cells to laser induced temperature shocks — •Anatol Fritsch, Tobias Kiessling, Roland Stange, and Josef Käs — Universität Leipzig, Leipzig, Germany

Living cells obtain mechanical stability from the cytoskeleton, a complex network of filamentous proteins, linkers and molecular motors. Alterations in cell mechanics to environmental stimuli, e.g. drug treatment, substrate stiffness, etc has been frequently investigated.

We developed a modified microfluidic Optical Stretcher setup able to adjust temperature during creep experiments on a millisecond timescale while automatically measuring thousands of cells. The features and reliability of this new tool are presented. A strong impact of temperature on single cell mechanics is revealed. Rarely investigated before, modulation of cell mechanics in response to temperature changes unexpectedly connects single cell mechanics to the rheology of polymer solutions.

BP 6.6 Mon 16:30 H 1028

Tailored Micro-Stencils for studying the impact of size and shape of migrating cell ensembles on their collective behavior — •Sebastian Rausch[1,2], Christian H. J. Böhm[1,2], and Joachim P. Spatz[1,2] — [1]Max Planck Institute for Intelligent Systems, Department of New Materials and Biosystems, Stuttgart — [2]Heidelberg University, Institute for Physical Chemistry, Heidelberg

Many fundamental biological processes, including morphogenesis, tissue repair and tumor invasion, require the collective motions of cells within groups, that are connected by cell-cell junctions.

The objective of our work is to elucidate and characterize the collective behavior of cell ensembles addressing the following key questions: To which extent are cell systems capable of developing multi-cellular collective patterns? How are collective properties established and controlled? We are thereby particularly interested in the formation of so called leader-cells and the specific impact of size and shape of a cell ensemble on its collective behavior and emergent properties.

Here, we introduce a tailored and adapted micro-stencil-technique based on soft-lithography, which allows us to create cell ensembles of arbitrary and well-defined shape and size. Our approach enables us to quantify the impact of these crucial boundary conditions. This technique enables us to improve the understanding of collective cell migration mode. Thorough knowledge of this fundamental migration behavior is a necessary prerequisite for a comprehensive understanding of morphogenesis or tumor metastasis via collective migration.

BP 6.7 Mon 16:45 H 1028

A theory of sarcomeric pattern formation by actin cluster coalescence — •Benjamin M Friedrich[1,3], Elisabeth Fischer-Friedrich[2,3], Nir S Gov[2], and Samuel A Safran[1] — [1]Department of Materials and Interfaces, Weizmann Institute of Science, Rehovot, Israel — [2]Department of Chemical Physics, Weizmann Institute of Science, Rehovot, Israel — [3]Current address: Max-Planck Institute for the Physics of Complex Systems, Dresden, Germany

Contractile function of striated muscle cells depends crucially on the almost crystalline order of actin and myosin filaments in myofibrils, but the physical mechanisms of myofibril assembly remains ill-defined. Passive diffusive sorting of actin filaments into sarcomeric order is kinetically impossible, suggesting a pivotal role of active processes in sarcomeric pattern formation. Using a computational model, we show that actin filament treadmilling in the presence of processive plus-end crosslinking provides a simple and robust mechanism for the polarity sorting of actin filaments. We propose that the coalescence of crosslinked actin clusters could be key for sarcomeric pattern formation. In our simulations, sarcomere spacing is set by filament length prompting tight length control already at early stages of pattern formation. The proposed mechanism could be generic and apply both to premyofibrils and nascent myofibrils in developing muscle cells as well as possibly to striated stress-fibers in non-muscle cells.

BP 6.8 Mon 17:00 H 1028

Probing the initial stages of phagocytosis with magnetic microparticles — •Matthias Irmscher[1], Arthur de Jong[1], Menno Prins[1,2], and Holger Kress[1] — [1]TU Eindhoven, Eindhoven, The Netherlands — [2]Philips Research, Eindhoven, The Netherlands

Phagocytosis, the uptake of external objects, such as bacteria is a key function of immune cells. It is a process that is driven by a deformation of the cell membrane with the aim of engulfing the target. The signaling pathways that drive phagocytosis have been extensively studied but little is known about the inherent mechanical aspects. We study the mechanics of phagocytosis by measuring the time-resolved changes of the membrane stiffness around a particle that acts as a phagocytic target. We use magnetic microparticles coated with immunoglobulin G to trigger phagocytosis upon binding. To quantify the translational and rotational motion of the magnetic particles, we tag them with fluorescent fiduciary markers. We exert a mechanical torque on the particles by applying a modulating magnetic field and simultaneously measure the rotational and translational particle displacements to quantify the mechanical properties of the binding site. Our measurements show an irreversible stiffening of the contact site by at least a factor five within a time span of a few hundred seconds. We hypothesize that the observed increase in stiffness originates from the cell membrane wrapping around the particle. By considering the energy of a deformed membrane, we describe the size of the phagocytic cup as a function of the measured stiffness. Our technique provides a new tool to quantitatively study the dynamics of membrane processes such as phagocytosis.

BP 6.9 Mon 17:15 H 1028

Mechanosensing of Type IV Pilus mediated Force in Epithelial Cells — •Enno Rainer Oldewurtel, Dirk Opitz, and Berenike Maier — Biozentrum, Universität zu Köln, Zülpicher Str. 47b, 50674 Köln

Mechanical stimuli can act as important cues in triggering signalling of cellular functions. The human pathogen *Neisseria gonorrhoeae* produces thin polymeric cell appendages called type-IV-pili (T4P). Retraction of these T4P can generate remarkably high forces and has been shown to be required for cytoskeletal changes (cortical plaques) in the host cell during infection.

Here, laser tweezers are used with T4P coated beads to mimic the mechanical stimulus of *N. gonorrhoeae* and to detect the forces required for the response. Cytoskeletal changes are monitored via fluorescent confocal imaging. We demonstrated a rapid cytoskeletal response to force generated by T4P. Both actin-EGFP and ezrin-EGFP accumulate beneath T4P-coated beads when force is applied exceeding controls without force or without pili within minutes.

Investigating possible mechanisms underlying this response we infected epithelial cells with *N. gonorrhoeae* and observed the distribution of other proteins tagged to fluorescent markers beneath bacterial micro-colonies. Vinculin, a typical focal complex protein, did not accumulate in cortical plaques. When adding RGD peptides in order to decrease a potential interaction between T4P and integrins, the formation of cortical plaques does not appear to be hindered. These results suggest a mechanism differing to the formation focal complexes.