BP 24: Cell adhesion and migration, multicellular systems I

Time: Thursday 9:30–13:00 Location: H11

Invited Talk BP 24.1 Thu 9:30 H11

Active motion in living systems: from molecules to assemblies of organisms — •Ben Fabry — Department of Physics, University of Erlangen-Nuremberg, Erlangen, Germany

The dynamics of active motion in living system is governed by intermittency and approach to kinetic arrest in striking analogy with inert non-equilibrium systems, including soft glasses and jammed colloidal assemblies. The emerging collective behavior of active agents, from molecules, cells, groups of cells up to the level of individual organisms, appears to depend on the shape and magnitude of the interaction potential between the agents and on the distance of the system's effective temperature from a critical point. These well-established concepts in condensed matter physics link dynamic interactions between the underlying elements to integrative biological functions at the macroscale, such as cytoskeletal arrangements at the leading edge of migrating cells, heterogeneity of immune cell migration, collective matrix invasion in metastasizing cancer cell assemblies, and the organization of penguin colonies.

BP 24.2 Thu 10:00 H11

Mechanics of tissue competition: Interfaces stabilize coexistence — Nirmalendu Ganai[1,2], •Tobias Büscher[1], Gerhard Gompper[1], and Jens Elgeti[1] — [1]Theoretical Soft Matter and Biophysics, Institute of Complex Systems, Forschungszentrum Jülich, 52425 Jülich, Germany — [2]Department of Physics, Nabadwip Vidyasagar College, Nabadwip, Nadia 741302, India

Cells grow and divide, which implies a change in volume. In physical terms, the conjugate force to a change in volume is pressure. Thus, in order to grow, cells must exert mechanical pressure on the neighbouring tissue. In turn, mechanical stress influences growth. This effect leads to a mechanical contribution when tissues compete for space. The tissue with higher homeostatic pressure, i.e. the pressure at which cell division and death balance, overwhelms the weaker one [2,3,4]. We expand these works to include different adhesion properties. Surprisingly, a weaker tissue can persist in stable coexistence with a stronger tissue, if adhesion between them is small enough. An analytic continuum description can quantitatively describe the underlying mechanism and reproduce the resulting pressures and cell-number fractions. Computer simulations furthermore display a variety of coexisting structures, ranging from spherical inclusions to a bicontinuous state.

[1] Ganai *et al*, 2018, arXiv:1809.10990
[2] Basan *et al*, 2011, *Phys. Biol.* **8**, 026014
[3] Podewitz *et al*, 2016, *EPL* **109**, 58005
[4] Podewitz *et al*, 2016, *New J. Physics* **18**, 083020

BP 24.3 Thu 10:15 H11

Interkinetic nuclear migration - a stochastic process constrained by tissue architecture — •Anne Herrmann[1], Afnan Azizi[2], Salvador J. R. P. Buse[2], Yinan Wan[3], Philipp J. Keller[3], William A. Harris[2], and Raymond E. Goldstein[1] — [1]Department of Applied Mathematics and Theoretical Physics, University of Cambridge, Cambridge, United Kingdom — [2]Department of Physiology, Development and Neuroscience, University of Cambridge, Cambridge, United Kingdom — [3]Howard Hughes Medical Institute, Janelia Research Campus, Ashburn, VA, USA

In developing pseudostratified epithelia, nuclei move repeatedly between the apical and basal surfaces of cells. This process is termed interkinetic nuclear migration (IKNM) and has been studied extensively in the brain, retina and spinal cord of multiple organisms. But despite these efforts many questions about the precise mechanism of IKNM remain. Based on *in vivo* light sheet microscopy we develop a quantitative model for the phenomenological properties of IKNM in the retinal system. Both the data and our model support the hypothesis of IKNM being a stochastic process during the majority of the cell cycle. Furthermore, our model reveals the remarkable and previously overlooked importance of simple physical constraints imposed by the overall tissue architecture. Because IKNM has been suggested to fulfil a regulatory role for retinal cell differentiation, our results have important implications for understanding proper eye development. Moreover, our findings will inform future work on IKNM in other organs and on the developmental regulation in these systems.

BP 24.4 Thu 10:30 H11

Continuum theory of bacterial aggregates — •Hui-Shun Kuan[1,2], Frank Jülicher[2], and Vasily Zaburdaev[1,2] — [1]Department of Biology, Friedrich-Alexander Universität Erlangen-Nürnberg, Erlangen, Germany — [2]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany

Cellular aggregates are common in many biological settings, ranging from bacterial biofilms to organoids and tumors. The dynamics of these systems is intrinsically non-equilibrium and driven by active processes in individual cells. In this work, motivated by *Neisseria gonorrhoeae* bacteria we develop a continuum theory to study bacterial aggregates driven by attractive pili-mediated forces and with excluded volume interactions. We describe the process of aggregate formation as an active phase separation phenomenon and identify the physics of the coalescence between two aggregates. In addition, within the same framework we can describe the demixing process of two bacterial types differing in the properties of their pili–pili interactions and thus can recover the patterns observed in experiments. Furthermore, this general hydrodynamic approach offers a way to incorporate the viscoelastic nature of the bacterial colonies and provide a link to the experiments focusing on material properties of cellular aggregates.

BP 24.5 Thu 10:45 H11

External forces generated by the attachment between blastoderm and vitelline envelope impact gastrulation in insects — •Stefan Münster[1,2,3], Alexander Mietke[2,3], Akanksha Jain[1], Pavel Tomancak[1], and Stephan Grill[1,2] — [1]MPI-CBG, Dresden — [2]TU Dresden, Biotec — [3]MPI-PKS, Dresden

Gastrulation is a critical step during the development of multicellular organisms in which a single-layered tissue folds into a multi-layered germband. This shape change is characterized by tissue folding and large-scale tissue flow. The myosin-dependent forces that underlie this process have been increasingly investigated; however, thus far, the possible interaction between the moving tissue and the rigid shell surrounding the embryo has been neglected. Here, we present our quantitative findings on the physical mechanisms governing gastrulation in the red flour beetle, Tribolium castaneum. We investigated the forces expected within the tissue given the myosin distribution observed by multi-view light-sheet microscopy and discovered that an additional external force must be counteracting this tissue-intrinsic contractility. We then identified that a specific part of the tissue tightly adheres to the outer rigid shell. This attachment is mediated by a specific integrin whose knock-down leads to a complete loss of the counter-force. Moreover, in the fruit fly Drosophila melanogaster, knock-down of another integrin leads to a severe twist of the germband, suggesting that the integrin-mediated interaction between tissue and vitelline envelope may be conserved in insects.

15 minutes break.

BP 24.6 Thu 11:15 H11

Complex fluid flow and cell polarity in the brain ventricular system — •Christian Westendorf[1], Shoba Kapoor[2], Yong Wang[1], Gregor Eichele[2], and Eberhard Bodenschatz[1] — [1]Max Planck Institute for Dynamics and Self-Organisation, Goettingen, Germany. — [2]Max Planck Institute for Biophyscial Chemistry, Goettingen, Germany.

Brain ventricles, that are filled with cerebrospinal fluid (CSF), are coated by specialized epithelial cells each of which carries a bundle of beating cilia. The cilia beats create complex and directional flow patterns that transport CSF and its constituents within the ventricles. The proximal cause of such an organized transport network rests on intricate domains of beating cilia [1]. We used antibody staining and DIC microscopy to explore ciliary polarity and dynamics in the domains and now show that the foundation of the organized flow within and across domains is grounded on the translational and rotational polarities of the cilia bundles. In areas of straight CSF flow, cilia are oriented in a uniform and unidirectional manner. In domains of circular flow, cilia in adjacent cells are oriented in their beating directions so as to generate a circular architecture. In cases where two flow domains are in opposite direction, the beating direction is opposite and changes abruptly over just a few cells. In conclusion, the complex transport

network in the ventricle is determined by the polarity properties of the ciliated cells and their cilia.

[1] R. Faubel, C. Westendorf, E. Bodenschatz and G. Eichele, Science 2016, 353(6295) p176-178.

BP 24.7 Thu 11:30 H11

Mechano-response and multicellular organization — •Sara Kaliman[1], Carina Wollnik[2], Damir Vurnek[1], Diana Dudziak[3], Florian Rehfeldt[2], and Ana-Suncana Smith[1] — [1]PULS group, Theoretical Physics I, Friedrich-Alexander-University, Erlangen — [2]3rd Institute of Physics - Biophysics, Georg-August-University, Göttingen — [3]Department of Dermatology, University Hospital, Friedrich-Alexander-University, Erlangen

Today, we know that mechano-response is one of the key regulators of a number of biological processes, including morphogenesis, cell differentiation and cancer progression. However, while there is good understanding of these effects in isolated cells, mechano-sensitivity in tissues remains heavily debated, and it remains unclear if tissue formation and individuals cells in a tissue are affected by surrounding rigidity. Here we show that mechano-response of multi-cellular colonies affects cell density in a steady state (homeostasis) as well as the cell density distribution within the colony. On the cellular level, decreasing substrate rigidity modulates cell proliferation and focal adhesions and induces switch from cuboidal to tubular epithelial structure. Surprisingly, despite strikingly different cell densities, different steady states are characterized by the same morphological features. On the other hand, tissues which are not in the steady state have different morphological properties. These results unequivocally relate cellular and macroscopic lengths scales in a tissue mechano-response.

BP 24.8 Thu 11:45 H11

Dynamics of vortices formed by active malaria parasites — •Pintu Patra[1], Anna Battista[1], Johanna Kratzer[2], Konrad Beyer[2], Astha Jaiswal[3], Karl Rohr[3], Friedrich Frischknecht[2], and Ulrich S. Schwarz[1] — [1]Institute for Theoretical Physics & BioQuant, Heidelberg University, Heidelberg, Germany — [2]Center for Infectious Diseases, Heidelberg University Medical School, Heidelberg, Germany — [3]Bioquant, University of Heidelberg & DKFZ, Heidelberg, Germany

Self-organised vortices can be observed in many biological systems, including schools of fish, groups of bacteria and active biopolymers. Here we study dynamic vortices formed by crescent-shaped Plasmodium sporozoites, the highly motile forms of the malaria parasite. Image processing of our experimental movies shows that the angular speed of sporozoites within a vortex is inversely proportional to their distance from the vortex centre, while their speed remains uncorrelated. Further, the distance of sporozoites from vortex centre is found to oscillate over time. To explain the characteristic features of sporozoite vortices, we develop an agent-based simulation, where each agent mimics the biophysical behaviour of an individual sporozoite. Our simulation shows that at high-density sporozoites can self-organize into vortices that recapitulate the experimentally observed features. Our quantification of motility statistics of sporozoites in the vortex state shows that vortex sporozoites are more dynamic than isolated sporozoites. Our study presents a new model system for the emergence of stable patterns by active particles with curved shapes.

BP 24.9 Thu 12:00 H11

Crawling to rolling: adhesion of malaria-infected red blood cells in shear flow — •Anil Kumar Dasanna[1] and Ulrich Sebastian Schwarz[2] — [1]Institute of Complex Systems (ICS-2), Forschungszentrum Jülich, Jülich, Germany — [2]BioQuant & Institute for Theoretical Physics, Heidelberg University, Heidelberg, Germany

During malaria infections, the adhesion of infected red blood cells (iRBC) in hydrodynamic flow is an essential step for parasite survival. The gradual change in morphology, stiffness and adhesiveness that takes place over the 48 hour cycle in the blood leads to complex adhesion dynamics in flow such as crawling, flipping and rolling. Earlier we have employed multiparticle collision dynamics for hydrodynamics combined with a deformable red blood cell model for simulating iRBC-adhesion in shear flow [1]. We now show that constant stiffening and change in the morphology drives the cells to unstable adhesion states whereas growth in the number of knobs works in the reverse direction, resulting in middle-stage infected cells to achieve stable adhesion in flow with maximum contact area with the substrate, which is essential for increasing the residency time in the vasculature. We summarize our findings in a phase diagram.

[1] Christine Lansche, Anil K. Dasanna et al., The sickle cell trait affects contact dynamics and endothelial cell activation in Plasmodium falciparum-infected erythrocytes, Nature communications biology 2018 (in press).

BP 24.10 Thu 12:15 H11

Parallelized Manipulation of Single Cell Behaviour with Magnetic Nanoparticles and Micromagnetic Arrays — Koceila Aïzel[1], •Cornelia Monzel[1,2], Elie Balloul[1], Chiara Vicario[1], Loïc Toraille[3], João Sampaio[4], Stanislas Rohart[4], Nicolas Vernier[5], Mathieu Coppey[1], Loïc Rondin[3], Jean-François Roch[3], and Maxime Dahan[1] — [1]Laboratoire Physico-Chimie, Institut Curie, Paris, France — [2]Experimental Medical Physics, Heinrich-Heine Univ., Düsseldorf, Germany — [3]Laboratoire Aimé Cotton, CNRS, Univ. Paris-Sud, ENS Cachan, Orsay, France — [4]Laboratoire de Physique des Solides, CNRS, Univ. Paris-Sud, Univ. Paris-Saclay, Orsay, France — [5]Centre de Nanosciences et de Nanotech., CNRS, Univ. Paris-Sud, Univ. Paris-Saclay, Orsay, France

The spatial manipulation of functionalized magnetic nanoparticles (MNPs) on subcellular scales is a powerful approach to probe and actuate biological processes in cells. In order to realize the manipulation of MNPs in a remote and well-defined manner, micromagnets are placed in the vicinity of the cell. The magnetic fields generated by these micromagnetic cuboids are quantified using optical magnetometry. Here, the spin properties of NV color centers in diamond enable determination of mT magnetic field distributions with micrometer sensitivity. We then arrange the micromagnets in arrays surrounded by cells, to realize a parallelized high-throughput manipulation. Using these arrays, we show that MNPs are efficiently redistributed in multiple cells and that functionalized MNPs can activate smallGTPases of cell signalling pathways.

BP 24.11 Thu 12:30 H11

Probing the interface structure of adhering cells by contrast variation neutron reflectometry — •Bert Nickel[1], Philip Böhm[1], Joachim Rädler[1], and Erich Sackmann[2] — [1]Fakultät für Physik & CeNS, Ludwig-Maximilians-Universität, 80539 München — [2]Physikdepartment E22, Technische Universität München, 85748 Garching

The cell substrate distance and the amount of water in the membrane substrate gap is difficult to determine. Here, we present a neutron reflectometry study of confluent epithelial cell monolayers on silicon substrates. The neutron experiments have been performed at MLZ in Garching, using MARIA and REFSANS, in collaboration with A. Koutsioubas and J.F. Moulin, respectively. The cell chamber enabled perfusion with cell medium and allowed for contrast variation in-situ by sterile exchange of buffer with different H2O-to-D2O ratio. Contrast variation reduces the ambiguity of data modelling for determining the thickness and degree of hydration of the interfacial cleft between the adherent cells and the substrate. Our data suggest a three-layer interfacial organization. The first layer bound to the silicon surface interface is in agreement with a very dense protein film with a thickness of 10 nm, followed by a highly hydrated 25 nm thick layer, and a several ten nm thick layer attributed to the composite membrane. Hence, the results provide clear evidence of a highly hydrated region between the composite cell membrane and the substrate.

BP 24.12 Thu 12:45 H11

The heat is on: Understanding germ granule segregation in *C. elegans* — •Anatol W. Fritsch[1], Matthäus Mittasch[1], Carsten Hoege[1], Frank Jülicher[2], Moritz Kreysing[1], and Anthony Hyman[1] — [1]MPI-CBG, Dresden, Germany — [2]MPI-PKS, Dresden, Germany

During embryonic development sexually reproducing species rely on the segregation of germ granules as one characteristic to specify their germ line. In *C. elegans*, P granules, a type of germ granule, have been found to behave as liquid-like protein condensates. The underlying biochemical control of the segregation has been described as an mRNA competition mechanism. Furthermore, it has been suggested that this drives segregation via spatially defined changes in the phase separation behavior of the condensates.

Using physical principles underlying phase separation, we are able to rescue the asymmetric localization of P granules in mutants with defective segregation *in vivo*. We replace wild type biochemical control with a localized temperature gradient that mimics its physical mechanism. Furthermore, with this approach, we are able to invert the endogenous spatial distribution of P granules in zygotes. This enables us to

study the dynamics of *in vivo* phase separation via controlled physical perturbations. In this study we conclude, that P granule segregation is a spatially tuned, diffusive-flux dependent, dissolution-condensation phenomenon.