BP 29: Multicellular Systems

Time: Tuesday 9:30–12:45 Location: H45

Invited Talk BP 29.1 Tue 9:30 H45

Cell Migration in Confined Geometries — •Joachim O. Rädler[1], Felix J. Segerer[1], Anna-Kristina Marel[1], Matthias L. Zorn[1], Christoph Schreiber[1], Peter Röttgermann[1], Alexandra Fink[1], Florian Thüroff[2], and Erwin Frey[2] — [1]Faculty of Physics and Center for NanoScience Ludwig-Maximilians-Universität München — [2]Arnold-Sommerfeld-Center for Theoretical Physics and Center for NanoScience, Faculty of Physics, Ludwig-Maximilians-Universität München

Epithelial cell migration is of prominent importance in wound healing, embryonic development, and cancer progression. Attempts to capture cellular hydrodynamics are currently progressing, yet it remains challenging to bridge multicellular motility to single cell migration. The talk intends to provide a perspective on how the study of cell migration in confining geometries facilitates and enhances the analysis of collective motility. Using time-lapse microscopy we study the directed flow of Madin Darby canine kidney (MDCK) cells in micro-channels. We also examine one of the hallmarks of active matter, the spontaneous emergence of vortices, in defined circular micropatterns with a fixed number of cells. The emergence of vortex states is reproduced by computer simulations based on a generalized Potts model. In agreement with experiment the model shows that vortex stability depends on the interplay of the spatial arrangement and internal polarization of neighboring cells. We will furthermore demonstrate that micropatterned surfaces allow the guidance of single cells and hence open up novel approaches to probe single-cell migration.

BP 29.2 Tue 10:00 H45

Dynamics of model cell monolayers — •Damir Vurnek[1], Sara Kaliman[1], Carina Wollnik[2], Florian Rehfeldt[2], Diana Dudziak[3], and Ana-Sunčana Smith[1,4] — [1]PULS group, Institute for Theoretical Physics I, FAU, Erlangen — [2]3rd institute of Physics - Biophysics, GAU, Göttingen — [3]University Hospital, Erlangen — [4]Division of Physical Chemistry, IRB, Zagreb

Morphogenesis and wound healing both require migration of a large number of constituent cells. This still unresolved problem of collective cell migration is addressed by using MDCK II model epithelium grown on collagen I coated glass substrates. We look at the global development of an initially droplet seeded system of cells which is allowed to expand freely over time. Large scale experiments spanning days and multiple connected fields of view are analyzed with particle image velocimetry of live fluorescent samples. This approach allows for both microscopic and macroscopic (millimeter) scales. As the whole edge, from the colony border up to the contact inhibited centre, is examined continuously new correlation length scales are uncovered. We analyze the connections between these scales and the perpetually increasing velocity of the colony border. Our recent findings push the limits of cooperative cell motion numbers into a previously unreported regime where thousands of cells act at the same time in a coordinated fashion.

BP 29.3 Tue 10:15 H45

Differential motility of *Neisseria gonorrhoeae* within bacterial micro-colonies determines the dynamics of colony merging — •Wolfram Pönisch[1], Christoph Weber[1], Khaled Alzurqa[2], Hadi Nasrollahi[2], Nicolas Biais[2], and Vasily Zaburdaev[1] — [1]Max Planck Institut für Physik Komplexer Systeme, Dresden, Germany — [2]Brooklyn College, New York, USA

Many bacteria possess type IV pili, several microns long filaments that protrude out of the cell membrane. Retraction of pili can generate pulling forces of up to 180 pN. These forces allow cells to attach and move over surfaces. Pili also mediate attractive cell-to-cell interactions that lead to the formation of microcolonies. In this project we examine microcolonies of *Neisseria gonorrhoeae*, the causative agent of the second most common sexually transmitted disease, gonorrhea. By tracking single cells inside of a microcolony, we were able to measure the mean square displacement of cells as a function of their position in a colony and to characterize their motility. We observe that cells close to the surface of the colony are considerably more motile than cells in the inner bulk. A simulation model of individual cells interacting via pili is used to unravel the mechanisms that cause this observation, for example by identifying differences in the number of interacting pili. We suggest that the position-dependent motility of cells in a colony determines the peculiar dynamics of merging microcolonies. The coalescence process is characterized by a fast approach of the colonies that is followed by a slow relaxation to the spherical shape.

BP 29.4 Tue 10:30 H45

Effect of flow and peristaltic mixing on bacterial growth in a colon-like geometry — •Jonas Cremer, Igor Segota, Markus Arnoldini, Alex Groisman, and Terence Hwa — University of California San Diego, 9500 Gilman Dr, La Jolla, CA 92093, USA

The large intestine harbors bacteria from hundreds of species with bacterial densities reaching up to 10^{12} cells per gram. Many different factors influence bacterial growth dynamics and thus bacterial density and microbiota composition. One dominant force is flow which can in principle lead to a washout of bacteria from the proximal colon. Active mixing by contractions of the colonic wall together with bacterial growth might counteract such flow-forces and allow high bacterial densities to occur. As a step towards understanding bacterial growth in the presence of mixing and flow, we constructed an in-vitro setup where controlled wall-deformations of a channel emulate contractions. We investigate growth along the channel under a steady nutrient inflow. In the limits of no or very frequent contractions, the device behaves like a plug-flow reactor and a chemostat respectively. Depending on mixing and flow, we observe varying spatial gradients in bacterial density along the channel. Active mixing by deformations of the channel wall is shown to be crucial in maintaining a steady-state bacterial population in the presence of flow. The growth-dynamics is quantitatively captured by a simple mathematical model, with the effect of mixing described by an effective diffusion term.

BP 29.5 Tue 10:45 H45

Predicting leaf growth by conformal map — •Karen Alim[1], Shahaf Armon[2], Eran Sharon[2], Boris I. Shraiman[3], and Arezki Boudaoud[4] — [1]Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany — [2]Racah Institute for Physics, Hebrew University, Jerusalem, Israel — [3]KITP, University of California, Santa Barbara, U.S.A. — [4]Laboratoire Reproduction et Développement des Plantes & Laboratoire Joliot-Curie, INRA, CNRS, ENS, Université de Lyon, Lyon, France

The dynamics and patterns of growth lie at the heart of morphogenesis, the shaping of an organ or organism. Here, we investigate the local growth throughout plant leaves. We perform a conformal map between the contours at successive stages during the growth of a leaf. Based on the mapping we predict the local displacement field in the leaf blade. The predicted displacement field agrees with the experimentally measured displacement field to 92%. The observed growth is not a mere dilation but dominated by a combination of dilation, rotation and reflection. Yet, we find that the complex growth characteristics are captured by a conformal map. The constraints implied by a conformal map on local growth dynamics suggest local regulation of growth at play.

30 min break

BP 29.6 Tue 11:30 H45

Biaxial nematic order in liver tissue — •Andre Scholich[1], Hidenori Nonaka[2], Hernán Morales-Navarrete[2], Fabián Segovia Miranda[2], Kirstin Meyer[2], Yannis Kalaidzidis[2], Marino Zerial[2], Benjamin Friedrich[1], and Frank Jülicher[1] — [1]Max-Planck-Institut für Physik komplexer Systeme, Dresden — [2]Max-Plank-Institut für Zellbiologie und Genetik, Dresden

Tissue cells typically exhibit an anisotropic distribution of membrane proteins that characterizes a structural polarity of the cell. This 'cell polarity' is linked to function, such as directed transport. In cellular monolayers and various epithelial tissues, cells are known to exhibit a vectorial cell polarity with distinct domains of apical and basal membrane proteins at opposite sides of the cell that face the two boundary surfaces of the flat tissue. Here, we analyze cells of a bulk tissue, the liver. We propose a concept of biaxial cell nematic to describe the distinct anisotropy of membrane proteins in hepatocyte liver cells. Analyzing high-resolution two-photon microscopy images of mouse liver, we find spatial patterns of aligned cell axes at the tissue scale. These spatial patterns characterize liver tissue as a biaxial nematic. Spatial

patterns are well-accounted for by a curvilinear reference system set by structural landmarks of large veins within the liver tissue. We discuss minimal mechanisms of cell-scale interactions that can account for the emergence of these tissue-scale patterns.

BP 29.7 Tue 11:45 H45

Driving forces of cellular arrangement during early embryogenesis of *Caenorhabditis elegans* — •Rolf Fickentscher, Philipp Struntz, and Matthias Weiss — University of Bayreuth, Bayreuth, Germany

We have studied mechanical cues in the early embryogenesis of the model organism *Caenorhabditis elegans* by means of a custom-made lightsheet microscope. This approach enabled us to acquire the trajectories and division axes/times of cells in embryos with fluorescently labeled nuclei over several hours. Furthermore, imaging membrane labeled embryos revealed cellular volumes and shapes as a function of time. In order to alter time and length scales during embryogenesis, we have used RNAi methods and different temperatures.

We had shown earlier that cellular trajectories can be modeled accurately in a purely mechanical framework during early embryogenesis [1], i.e. early cell organization is determined by the cells' quest for a position with least repulsive interactions among themselves and the eggshell. By altering the temperature, we show now that cellular velocities in the embryo exhibit an Arrhenius-scaling. Hence biochemical processes like adhesion and remodeling of the cytoskeleton determine the forces which then drive cellular motion. Furthermore, our data highlights a correlation between cell volumes and the respective cell-cycle durations. Based on our experimental data, we propose a minimal model for this phenomenon and relate it to observations in RNAi-treated animals.

[1] R. Fickentscher, P. Struntz & M. Weiss, Biophys. J, **105** (2013)

BP 29.8 Tue 12:00 H45

Tissue level optical benefits of photoreceptor nuclei inversion — •Kaushikaram Subramanian[1], Zuzanna Blaszczak[2], Alfonso Garcia Ulloa[1], Martin Weigert[1], Irina Solovei[4], Jochen Guck[3], and Moritz Kreysing[1] — [1]MPI-CBG, Dresden, Germany — [2]Cavendish Lab, Cambridge Univ, UK — [3]BIOTEC, TU Dresden, Germany — [4]Dept of Biology, LMU Munich, Germany

With the photoreceptor cells lying at the back, the retina has a counter intuitive optical design that necessitates propagation of light through hundreds of microns of neural tissue prior to detection. Retina has a high cell density (3-5 times higher than brain) and a large volume-fraction of nuclei that can potentially scatter light. During postnatal retinal development the photoreceptor nuclei in nocturnal mammals invert their chromatin architecture [1]. Based on interferometric measurements and simulations, it was suggested that scattering in the retina is reduced by this chromatin re-arrangement and that the individual nuclei possess the optical quality of lenses [2]. Subsequently, predictions about light transmission at tissue level were made. Using the concept of modulation transfer we aim to experimentally verify the simulation based predictions on tissue level optical benefit stemming from this nuclear inversion. Specifically we will present a comparative optical characterisation of wild type and a transgenic mice retina lacking inverted nuclei. Further results indicate optical quality of the retina improve during terminal retinal development, the period in which the unique inversion of nuclei takes place. References: [1] Solovei et al, Cell, 137(2) (2009) [2] Błaszczak et al, Opt Express, 22(9) (2014)

BP 29.9 Tue 12:15 H45

Mechanosensitive regulation of cell extrusions during pupal morphogenesis of the fly wing — •Marko Popovic[1], Raphael Etournay[2], Franz Gruber[2], Matthias Merkel[1], Amitabha Nandi[1], Corinna Blasse[2], Gene Myers[2], Guillaume Salbreux[1], Suzanne Eaton[2], and Frank Julicher[1] — [1]Max Planck Institute for Physics of Complex Systems, Dresden — [2]Max Planck Institute of Molecular Biology and Genetics, Dresden

The fly wing is a double layered epithelium which significantly reshapes during pupal stages of development. Cell extrusion is a process by which cells are expelled from the epithelium. It allows the tissue to reduce the number of cells during pupal development and thus to adjust the stress in the tissue. Although extrusion rates are reproducible in wild type experiments they exhibit quantitatively different behavior in genetically and mechanically perturbed wings. How the extrusions are controlled is yet unknown. Motivated by the experimentally obsevred extrusion patters we construct a model of mechanosensitive regulation of cell extrusions. In combination with a simple continuum model, previously used to describe the fly wing development [Etournay et. al. eLife 2015], it yields a dynamical equation for extrusion rates with a single relaxation time-scale.

BP 29.10 Tue 12:30 H45

Accumulation of mutations for tumour initiation: extreme value statistics in a neutral Moran process — •Philip Greulich[1,2] and Benjamin D. Simons[1,2] — [1]Cavendish Laboratory, University of Cambridge, Cambridge, UK — [2]Gurdon Institute, University of Cambridge, Cambridge, UK

To initiate tumour growth, usually several mutations need to accumulate in at least one tissue cell. Some mutations may be (quasi-) neutral alone, but the epistatic interplay of a critical number of neutral mutations may lead to a selective advantage over normal cells, which can trigger tumour growth. Here I study a model for neutral competition of renewing tissue (stem) cells which accumulate random neutral mutations over time (Moran process). The quantity of interest is the "tumour-initation risk", the probability that at least one cell acquires a threshold number of mutations, which is supposed to trigger further events towards tumour progression. By studying the extreme value statistics of mutation numbers, which are correlated between related cells, I show how this risk scales with the tissue size and with time. Thereby, I will reason how neutral competition of stem cells can reduce the risk of tumour initiation compared to non-competitive stem cells that divide only through asymmetric divisions.