BP 36: Cell adhesion, mechanics and migration II

Time: Wednesday 15:00–18:30 Location: H 1058

BP 36.1 Wed 15:00 H 1058

The mechanics of invasion: How contraction sets the stage for invasive migration. — Katarzyna Kopanska and •Timo Betz — Physical-Chemistry Curie, UMR168, Institut Curie, Paris, France

To move out of the primary tumor, cancer cells start a complex process of migration in the surrounding tissue called invasion. Understanding the mechanisms responsible for the onset of cancer cell invasion remains an urgent research subject on the path to new strategies to prevent malignant invasion, and thus improve the prognosis of many cancer types. We focus on the mechanical events that can be observed before and during invasion of the colon cancer cell line CT26. The experimental system consists of a spheroid of about 2000 cells that is embedded in a collagen I matrix. Before the onset of invasion, a contraction of the collagen gel is observed that shows 3 different phases. Our results suggest that an increase in mechanical tension within the collagen matrix facilitated the outgrowth of cells and hence triggers invasion. In this sense, the cells in the spheroid may optimize the mechanical properties of their environment via force application to facilitate invasion.

BP 36.2 Wed 15:15 H 1058

Forces and flows in adhesion-independent cell migration — •Anna Erzberger[1], Martin Bergert[2,3], Ewa Paluch[3], and Guillaume Salbreux[1] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]currently at: Laboratory of Thermodynamics in Emerging Technologies, ETH Zuerich, Switzerland — [3]MRC Laboratory for Molecular Cell Biology, UCL, London, UK

When cells move using specific substrate adhesions, they pull in the direction of motion with large stresses that contract the substrate. In confined environments however, cells exhibit directed migration modes which are independent of specific adhesions. Here, we combine hydrodynamic theory and experiments on motile cancer cells to investigate the forces involved in adhesion-free migration. We show that actin cortex flows and deformations move the cells via non-specific substrate friction. Strikingly, the forces propelling the cell forward are several orders of magnitude lower than during adhesion-based motility, while achieving similar cell velocities. Moreover, the force distribution in adhesion-free migration is inverted: it acts to expand, rather than contract, the cell substrate in the direction of motion. We discuss the implications of this fundamentally different mode of force transduction for cell-cell and cell-substrate interactions during migration.

BP 36.3 Wed 15:30 H 1058

Experimental Exploration of the Phase Space of Actin Waves — •Erik Bernitt, Malte Ohmstede, and Hans-Günther Döbereiner — Institut für Biophysik, Universität Bremen, Bremen, Germany

We study actin waves in fibroblast cells that noticeably undulate the cell surface forming Circular Dorsal Ruffles (CDRs). We are interested in the currently unknown mechanism underlying these waves. Previous research in our lab revealed that the cell shape strongly influences the wave dynamics of CDRs, which complicated an analysis of the wave mechanism due to the irregular morphology of fibroblasts. When forced into a well-defined, disk-like morphology, however, cells form waves in a highly regular manner allowing detailed studies of the wave mechanism. We place these cells in flow channels allowing for rapid switching of the cellular biochemical state.

We ask which active role actin plays in the propagation mechanism of CDRs. From the behavior in the phase space of theoretical models, we expect that the amount of free g-actin plays a pivotal role. Our setup gives us access to this phase space experimentally. With our approach, experimental and theoretical data can easily be matched, because CDRs on disc-shaped cells propagate laterally between cell edge and nucleus, forming an effectively one-dimensional system with periodic boundary conditions. Here we report our latest experiments in which we shift the cell's position of the chemical equilibrium between f- and g-actin using latrunculin A.

BP 36.4 Wed 15:45 H 1058

Catching a target with directed run and tumble motion — •Pawel Romanczuk[1] and Guillaume Salbreux[2] — [1]Dept. of Ecology and Evolutionary Biology, Princeton University, NJ 08544 — [2]Max Planck Institute for the Physics of Complex Systems, 01187 Dresden

During Zebrafish development progenitor cells are required to arrive with high temporal and spatial precision at specific targets sites. On the one hand this directed migration is associated with the presence of chemical cues, and on the other hand it was reported to consist of phases of persistent motion ("runs") interrupted by reorientation events associated with cell repolarization ("tumbles") [1]. Here we consider a minimal model of chaser particles undergoing directed migration towards a target with noisy information on the target position, e.g. due to chemotactic sensing. The chaser moves by switching between two phases of motion (run and tumble), reorienting itself towards the target during tumble phases, and performing a persistent random walk during run phases. We show that the chaser average run time can be adjusted to minimize the catching time or the spatial dispersion of the chasers. We obtain analytical results for the catching time and for the spatial dispersion in the limits of small and large ratios of run time to tumble time, and scaling laws for the optimal run times. Finally, we discuss the possibility of an optimal chemotactic strategy in animal cell migration by analyzing in-vivo experiments together with simulation of a more detailed stochastic model fitted to experimental data.

[1] M. Reichman-Fried et al., Developmental Cell 6, 589 (2004)

BP 36.5 Wed 16:00 H 1058

Bistable forespore engulfment in *B. subtilis* by a zipper mechanism in absence of the cell wall — •Nikola Ojkic[1], Javier López Garrido[2], Kit Pogliano[2], and Robert G. Endres[1] — [1]Department of Life Sciences, Imperial College, London, United Kingdom — [2]Division of Biological Sciences, University of California, San Diego, La Jolla, California, USA

To survive starvation, the bacterium *Bacillus subtilis* forms durable spores. The initial step of sporulation is asymmetric cell division, leading to a large mother-cell and a small forespore compartment. After division is completed, the mother cell engulfs the forespore in a slow process based on cell-wall degradation and synthesis. However, recently a new cell-wall independent mechanism was shown to significantly contribute, which can even lead to fast engulfment in ~ 60 % of the cases when the cell wall is removed. In this backup mechanism, strong ligand-receptor binding between mother-cell protein SpoIIIAH and forespore-protein SpoIIQ leads to zipper-like engulfment, but quantitative understanding is missing. We combined florescence image analysis and stochastic Langevin simulations of the fluctuating membrane to investigate the origin of fast bistable engulfment in absence of the cell wall. We predict regions of osmotic pressure and membrane-surface tension that produce successful engulfment. Our cell morphologies compare favorably with experimental time-lapse microscopy, with engulfment sensitive to the number of SpoIIQ-SpoIIIAH bonds in a threshold-like manner. Indeed, decreasing the medium osmolarity in experiments prevents engulfment in line with predictions.

BP 36.6 Wed 16:15 H 1058

Modeling crawling cell motility — •Jakob Löber[1], Falko Ziebert[2], and Igor Aranson[3] — [1]Institut für Theoretische Physik, TU Berlin — [2]Albert-Ludwigs-Universität, Freiburg, Germany — [3]Argonne National Laboratory, Argonne, USA

Self-propelled motion, emerging spontaneously or in response to external cues, is a hallmark of living organisms. Self-propulsion relies on the force transfer to the surrounding. While self-propelled swimming in the bulk of liquids is fairly well characterized, many open questions remain in our understanding of self-propelled motion of cells along substrates. Here we present a phenomenological model for crawling cells based on an advected phase field model and other reaction-diffusion equations. The force transfer from the cell to the substrate is explicitly taken into account, giving rise to complex modes of cell movement such as bipedal motion and stick-slip motion. The model captures the generic structure of the traction force distribution and faithfully reproduces experimental observations, like the response of a cell on a gradient in substrate elasticity (durotaxis). Collective states of motion such as concerted rotation arises for multiple interacting cells on patterned substrates.

30 min break

BP 36.7 Wed 17:00 H 1058

Spontaneous actin dynamics in contractile rings — Viktoria Wollrab[1,2], Raghavan Thiagarajan[1,2], Daniel Riveline[1,2], and •Karsten Kruse[3] — [1]Laboratory of Cell Physics, Institut de Science et d'Ingénierie Supramoléculaires, 67083 Strasbourg, France — [2]Laboratory of Cell Physics, Institut de Génétique et de Biologie Moléculaire et Cellulaire, 67404 Illkirch, France — [3]Theoretische Physik, Universität des Saarlandes, 66123 Saarbrücken, Germany

Networks of polymerizing actin filaments are known to be capable to self-organize into a variety of structures. For example spontaneous actin polymerization waves have been observed in living cells in a number of circumstances, notably, in crawling neutrophils and slime molds. During later stages of cell division, they can also spontaneously form a contractile ring that will eventually cleave the cell into two daughter cells. We present a framework for describing networks of polymerizing actin filaments, where assembly is regulated by various proteins. It can also include the effects of molecular motors. We show that the molecular processes driven by these proteins can generate various structures that have been observed in contractile rings of fission yeast and mammalian cells. We discuss a possible functional role of each of these patterns.

BP 36.8 Wed 17:15 H 1058

Characterizing Cell Motility and Transmigration on Ring Shaped Micro Patterns — •Christoph Schreiber, Felix Jakob Segerer, and Joachim Oskar Rädler — Fakultät für Physik, Ludwig-Maximilians-Universität München, Germany

Cell migration is important in many biological processes such as embryogenesis, wound healing, or cancer metastasis. To understand the formation of tumors and the effect of drugs, a detailed characterization of the migration behavior is important. Furthermore the ability to overcome barriers like the basement membrane is a key indicator for the aggressiveness of different cancer cells. Therefore a systematic approach for studying transmigration behavior is necessary to characterize the invasiveness of cancer cells.
Here, we study single cell migration constrained to a micro-patterned ring-shaped lane. On such tracks cells perform a 1D persistent random walk like movement that can be divided in a directional and a reorientation phase. Analyzing large arrays in parallel, we are able to evaluate characteristic velocities and persistence times of a cell line with high accuracy. By introducing a gap of defined size and chemical composition in the ring shaped lane we study how cell migration is affected by the encounter with a chemical barrier. At the chemical border cells either turn around or transmigrate over the barrier. Studying the transmigration probability systematically, we find a steady decrease of transition probability with increasing barrier width.

BP 36.9 Wed 17:30 H 1058

Is the wound healing mechanism an accelerating one? — •Damir Vurnek, Sara Kaliman, and Ana-Sunčana Smith — Theoretical Physics I, FAU Erlangen

Morphogenesis and wound healing both require migration of large number of constituent cells. We address these problems by using MDCK II model epithelium grown on collagen I coated glass substrates. Usually, to study such a system, a part of an expanding monolayer is carefully analyzed. Here we take the complementary approach and look at the global development of an, initially droplet seeded, system of cells which is allowed to expand freely over time. In contrast to most studies majority of our experiments performed have very long time windows of at least 10 days. On the basis of experimental findings the known model of exponential growth of small ($< 0.1\text{mm}^2$) cell clusters is expanded with an additional parameter which accounts for the slowing down of area growth. Thus, with the use of a simple differential equation, and easily interpreted parameters - initial colony area (A_0), colony doubling time (τ) and effective slowing down of growth (b) - one can successfully predict the area expansion of clusters in the range of four orders of magnitude. Further data analysis shows a stunning picture of a perpetually accelerating monolayer edge, in stark opposition to the concept of constant speed limits supposedly reached by macroscopic ($> 10\text{mm}^2$) monolayers. These findings raise the questions of accumulating stress levels such epithelial tissues endure before breaking or buckling, or even just slowing down.

BP 36.10 Wed 17:45 H 1058

Migration patterns of dendritic cells in response to chemokines — •Veronika Bierbaum, Jan Schwarz, Eva Kiermaier, Michael Sixt, and Tobias Bollenbach — IST AUSTRIA, Am Campus 1, 3400 Klosterneuburg

Dendritic cells are key components of the adaptive immune system. They navigate through tissues by sensing two different chemokines, CCL19 and CCL21. We develop a physical description of dendritic cell migration as a function of the surrounding chemokine field formed by both immobilized and soluble chemokines. We perform in vitro assays to characterize key properties of cell motion. In these assays, cells are exposed to well-controlled concentration profiles of the two chemokines. We monitor the gradients and the cellular motion using time-lapse microscopy and obtain a large number of cell trajectories. These trajectories are well captured by Langevin equations, enabling us to separate the stochastic and deterministic contributions to cell motion. In soluble gradients of CCL19 and CCL21, dendritic cells maintain their directionality towards the chemokine source over a large range of concentrations. However, in linear and exponential gradients of immobilized CCL21 the cells' directionality depends on chemokine concentration and is maximal at low concentrations. To rationalize these observations we develop a theoretical model of chemokine signal detection and interpretation. This experimental-theoretical approach can reveal general principles of cell migration in response to chemokines.

BP 36.11 Wed 18:00 H 1058

Stress induced collective cell migration in epithelial sheets — •Michael Köpf — Departement de Physique, Ecole Normale Superieure Paris, France

Stress normal to the boundary of an epithelial sheet can arise in constrained and unconstrained cell layers through pushing and pulling of surrounding tissue and wettability of the substrate, respectively. A continuum model describes the epithelium as a polarizable and chemomechanically interacting layer under the influence of such stresses. This model links the experimentally observed formation of finger-like protrusions at the edge of unconstrained spreading cell monolayers to substrate wettability [1]. Statistics of the velocity orientation shows a strong alignment in the fingers opposed to an isotropic distribution in the bulk, in agreement with measurements by Reffay et al [2]. The model further exhibits a stress accumulation within the tissue that proceeds in form of a mechanical wave, starting at the wound edge [3].

Additionally, four types of spreading and motility can identified, depending on the normal stress at the boundaries: Uniform deformation, non-uniform deformation, uniform gliding and peristaltic (*worm-like*) progression. Analytical and numerical solutions are presented along with bifurcation diagrams using normal stress and active force as control parameters [4].

[1] Köpf, Pismen, *Soft Matter* **9** (2013) 3727-3734
[2] Reffay et al., *Biophysical Journal* **100** (2011) 2566-2575
[3] Serra-Picamal et al., *Nature Physics* **8** (2012) 628-634
[4] Köpf (2014) in preparation

BP 36.12 Wed 18:15 H 1058

Polarization of motile amoeboid cells under confinement — •Oliver Nagel[1], Can Guven[2], Matthias Theves[1], Megan Driscoll[2], Wolfgang Losert[2], and Carsten Beta[1] — [1]Institute of Physics and Astronomy, University of Potsdam, Germany — [2]Department of Physics, University of Maryland, College Park, Maryland, USA

The typical environment of motile eukaryotic cells, like leukocytes, cancer cells, and amoeba, is dominated by the narrow interstitial spacings of tissue or soil. While most of our knowledge of actin-driven eukaryotic motility is based on cells that move on planar open surfaces, recent work has demonstrated that confinement can lead to strongly altered motile behavior. Our experiments show that motile amoeboid cells undergo a spontaneous symmetry breaking under confinement. Cells inside narrow channels switch to a highly persistent, unidirectional mode of motion, moving at a constant speed along the channel. They remain in contact with the two opposing channel side walls and alternate protrusions of their leading edge near each wall. The actin cytoskeleton of the cells exhibits a characteristic arrangement that is dominated by dense, stationary actin foci at the side walls, together with less dense dynamic regions at the leading edge. Our experimental findings can be explained based on an excitable network model that accounts for the confinement-induced symmetry breaking and correctly recovers the spatio-temporal pattern of protrusions at the leading edge.