AKB 5 Cell Motility II

Time: Monday 14:00–15:45 Room: ZEU 255

Invited Talk AKB 5.1 Mon 14:00 ZEU 255

Cell motility as persistent random motion: theories from experiments — •Henrik Flyvbjerg[1,2], David Selmeczi[2,3], Stephan Mosler[2], Peter H. Hagedorn[1], and Niels B. Larsen[1,2] — [1]Biosystems Department, Risø National Laboratory, DK-4000 Roskilde, Denmark — [2]Danish Polymer Centre, Risø National Laboratory, DK-4000 Roskilde, Denmark — [3]Department of Biological Physics, Eötvös Loránd University, H-1117 Budapest, Hungary

Cell migration is essential in many physiological and pathological processes and in emerging medical technologies that depend on it for colonization of biomaterials. Quantitative migration studies rely on motility models for data interpretation. Finding no model in the literature that captures the nature of our data, we used the data to capture the nature of suitable models. An analysis of trajectories followed by motile human keratinocytes and fibroblasts lead to cell-type-specific motility models. These models show that cells have memory, and apparently reflect the cells' different roles in the organism. The method of analysis is general and may be applied to other motile cell-types and organisms.

AKB 5.2 Mon 14:30 ZEU 255

A biomimetic model system shedding light on active lamellipodial biomechanics — •Björn Stuhrmann[1], Florian Huber[1], Thomas Rudolph[2], Klaus Zimmer[2], and Josef Käs[1] — [1]Institute for Soft Matter Physics, University of Leipzig, Linnéstr. 5, 04103 Leipzig, Germany — [2]Leibniz-Institut für Oberflächenmodifizierung e.V., Permoserstr. 15, 04303 Leipzig, Germany

In cells displaying crawling motility, cell boundary advancement is governed by the assembly of actin protein, tightly regulated by a wealth of accessory proteins. The key molecular players involved in these processes have been identified [1] and are used in this project to build a minimal model system of the cell lamellipodium. A polymerizing actin gel representing the lamellipodium is generated in nanostructured, cell-sized chambers. System confinement to cellular volumes is a crucial step towards cellular conditions and distinguishes our approach from existing assays. In the presence of ATP, the emerging gel represents for the first time a self-sustaining, polymerizing machine mimicking the cell lamellipodium *in vitro*. Offering the possibility to selectively change biochemical and physical parameters and to study the system's response in terms of its structural, dynamical and rheological properties, this model system presents a novel means to explore biomechanical mechanisms underlying cell motility.

[1] Loisel TP, Boujemaa R, Pantaloni D, Carlier MF. Nature. 1999 Oct 7;401(6753):613-6.

AKB 5.3 Mon 14:45 ZEU 255

Measuring protrusion forces of locomoting cells — •Marcus Prass[1], Ken Jacobson[2], and Manfred Radmacher[1] — [1]Institute of Biophysics, University of Bremen, 28359 Bremen, Germany — [2]Dept. of Anatomy and Cell Biology, University of North Carolina, Chapel Hill, USA

Cell migration is very important for cellular processes like wound healing or metastasis. Although much is known from the biological point of view on the actin-myosin machinery involved in cell migration, the exact mechanism of force generation is still unclear. One possible mechanism of force generation is the polymerization ratchet model. Here, thermal fluctuations of actin filaments are necessary for polymerization of actin filaments. Since this process effectively converts chemical energy in mechanical energy a protrusive force is generated. We have designed a cantilever-based instrument to measure directly protrusion forces at the leading edge of migrating cells. An AFM-cantilever oriented perpendicular to the substrate is deflected by a migrating keratocyte (epithelial cell prepared from trout scales). The deflection could be measured by video microscopy or at better temporal and spatial resolution using a position sensitive detector. The distance between cantilever and substrate was approximately 80 nm to guarantee that the leading edge of the lamellipodium was investigated. We will show first experimental results and discuss them in the context of existing theories.

AKB 5.4 Mon 15:00 ZEU 255

Investigation and Manipulation of Membrane Dynamics by an Optical Tweezers Technique — •Michael Goegler, Timo Betz, and Josef Käs — Institute for Soft Matter Physics, University of Leipzig, Linnéstrasse 5, 04103 Leipzig, Germany

Cell migration is essential in various cellular activities, such as morphogenesis, wound healing, and metastasis. In these events, protrusion of the cell membrane at the leading edge is the fundamental step, and the mechanism driving this movement is likely associated with the elongation of polymerizing actin filaments or with molecular motors, such as myosin. To elucidate the mechanism of protrusion, we use a new laser based technique to study membrane motion with high spatial and temporal resolution in the nanometer and microseconds range, respectively. A diffraction limited laser spot is positioned at the leading edge of a cell and the forward scattered light is imaged on a quadrant diode detector which serves as a position sensitive device. We investigated the membrane motion at the leading edge of different cell types, such as fibroblasts and erythrocytes. The new technique has the potential to reveal relative contributions to the membrane fluctuations based on its frequency spectrum, and to measure physical properties, such as the bending rigidity of the membrane. By increasing the laser intensity we were able to exert a significant force on the cell's leading edge that is strong enough to deform the cell and change its membrane dynamics. We present the capabilities of the technique and show that it provides the opportunity to measure rheological properties of cells.

AKB 5.5 Mon 15:15 ZEU 255

Protrusion Forces Driving Rapidly Translocating Cells — •Michael Goegler[1], Claudia Brunner[1], Allen Ehrlicher[1], Bernd Kohlstrunk[1], Detlef Knebel[2], and Josef Käs[1] — [1]Institute for Soft Matter Physics, University of Leipzig, Linnéstrasse 5, 04103 Leipzig, Germany — [2]JPK Instruments AG, Bouchéstrasse 12, 12435 Berlin, Germany

Cell motility is a fundamental process of many phenomena in nature, such as immune response, wound healing, and metastasis. Mechanisms of force generation for cell migration have been described in various hypotheses requiring actin polymerization and/or molecular motors, but quantitative force measurements to date have focused on traction forces. Here we present a direct measurement of the forward force generated at the leading edge of the lamellipodium and at the cell body of a translocating fish keratocyte. We positioned an elastic spring, the cantilever of a scanning force microscope (SFM), in front of a moving cell, which pushed the cantilever out of its path. The forward force was calculated using the detected vertical deflection of the cantilever in an "elastic wedge model", which considers cellular deformation. We measured forward forces between 1-8 nN without visibly affecting the cells. At stronger opposing forces up to at least 15 nN the lamellipodium of the cell retracted locally whereas the overall movement of the cell remained unaffected. Measurements with steadily increasing applied force were carried out to determine a load dependence behaviour. We investigated the effect of cytochalasin D in force measurements to elucidate the importance of actin polymerization in cellular protrusion.

AKB 5.6 Mon 15:30 ZEU 255

Lateral Membrane Waves Constitute a Universal Dynamic Pattern of Motile Cells within the Animal Kingdom — •H.-G. Döbereiner[1,2], B. J. Dubin-Thaler[1], J. Hofman[3], H. S. Xenias[1], T. N. Sims[4], G. Giannone[1], M. L. Dustin[4], C. Wiggins[3], and M. P. Sheetz[1] — [1]Biological Sciences, Columbia University, New York — [2]Physics, Columbia University, New York — [3]Applied Physics, Columbia University, New York — [4]Skirball Institute, New York University School of Medicine, New York

Cell motility is driven by actin polymerization and myosin motor activity. We have monitored active movements of the cell circumference using quantitative differential interference contrast and total internal reflection fluorescence microscopy. Spreading and motility essays were done on specifically adhesive substrates for a variety of cells including mouse embryonic fibroblasts and T-cells, as well as wing disk cells from drosophila melanogaster. Despite their functional diversity, all those cell types exhibit similar dynamic patterns in their normal membrane velocity. In particular, we found that protrusion and retraction activity is organized

in lateral waves running along the cell circumference with speeds on the order of 100 nm/s. These wave patterns show both spatial and temporal long-range periodic correlations reflecting a corresponding organization of the actomyosin gel. These lateral waves seem to be quite a general phenomenon, since we found them in two different cell types of the mouse, a mammal, and in one cell type of the common fruit fly, an insect. Thus, we encounter a universal motility pattern across different phyla within the animal kingdom.