

modulates the transition boundaries between various equilibrium phases, as well as the kinetic glass transition density. We also study the effects of motorization using a modeled kinetic rate that couples the chemical response to mechanical environment.

1640-Pos Board B550

Using Magnetic Twisting Cytometry to Study Monocyte Activation

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Circulating monocytes are key blood cells in a variety of disorders of the immune system. They are critically involved in the development of atherosclerotic lesions due to their ability to leave the blood stream and differentiate into macrophages upon entering sub-endothelial space. Prior to leaving the blood stream, a combination of chemokines triggers activation pathways which result in an increased expression of integrins.

We are investigating whether the activation-dependent recruitment of integrins influences the mechanical properties of the cells. Besides getting new insights into basic cellular mechanics, this research also aims to lay the foundation for future cell biosensors for the diagnosis of cardiovascular disease.

We have immobilized human monocytic leukemia cells (THP-1 cells) on glass substrates that support binding via the Fc-receptor. The viscoelastic properties of the cells were quantified by exerting a sinusoidal torque via magnetic particles bound to membrane protein CD14. We recorded the translational response of single cells and deduced the storage and loss moduli of THP-1 cells for several orders of magnitude of the actuation frequency. We will present the influence of pro-inflammatory ligands on the viscoelastic properties of the cells.

1641-Pos Board B551

Regulation of Cell-Surface Adhesion During Amoeboid Migration

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During amoeboid migration, cell-substrate interactions play a critical role by supplying the traction allowing a cell to move itself forward. It has been shown that the ability of individual mammalian cells to move will depend on their adhesiveness to that surface, with moderately adhesive surfaces being ideal: moderate adhesion allows cells to gain traction to move forward while still permitting detachment of the cell rear. In addition to cell-substrate adhesion, migrating cells often experience cell-cell adhesion, and in many systems (such as wound healing or embryogenesis) such adhesion can dominate. The amoeba *Dictyostelium discoideum* naturally exhibits both cell-substrate and cell-cell adhesion during the aggregation process. We used both high- and low-magnification time-lapse microscopy to investigate the individual and collective migration of *D. discoideum* on substrates of varying adhesiveness, as well as on interfaces between substrates. We find that non-ideal adhesive surfaces can affect both individual cell migration as well as the behavior of cell groups. At the population scale, non-ideal surfaces slow down the initiation of aggregation and change how the process is performed: instead of forming large aggregation centers, the population forms small aggregation centers which coarsen over time until the standard aggregation center size is eventually reached. At the scale of single cells, we measure both adhesion ability as well as the area of contact between cells and surface for individual cells and cells that are part of groups. On all surfaces the contact area oscillates, reflecting the migration dynamics. Surprisingly, comparable forces are needed to rip cells off all surfaces, indicating that surface adhesion may be regulated by the cells.

1642-Pos Board B552

Dynamics of Wound Repair in the Lamellipodia

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Cells are able to recover from mechanical injuries to their plasma membrane and cortical cytoskeleton. The dynamics of cell recovery after injury may illuminate specific mechanisms of injury repair and also help understand how the normal cell organization and shape are maintained. We use a model system of fish keratocytes, epidermal cells likely sustaining frequent injury *in vivo*, to investigate the dynamics of wound closure. The advantage of these cells are their flat, large, and regularly-shaped lamellipodia, where wounds of well-defined shape can be produced and quantified. A glass micro-needle was applied to induce either external cuts (cutting the lamellipodia from its edge) or internal holes (not reaching the cell edge) in the lamellipodia. Both types of wounds closed in a few seconds by means of *de novo* assembly of the actin network from the wound edges towards its interior. We compared the rates of wound closure depending on the wound shape, and the direction of closure with respect to the direction of cell motion. In most cases, the wound closure rate was highest in the direction of cell migration and lowest in the opposite direc-

tion, irrespective of wound location, indicating the presence of cell-polarity cues throughout the lamellipodia and not just at its front edge. Inhibition of myosin II activity with blebbistatin did not prevent wound closure, but appeared to diminish the front/back bias in the closure rate, indicating that myosin II was not necessary for repair, but may contribute to the polarity cues. To get insight into the role of membrane tension in repair, we are currently analyzing the dependence of closure on the shape and curvature of the wound edge. Supported by NSF grant 3100A0-112413 and a Swiss SystemsX.ch IPHD fellowship.

1643-Pos Board B553

Adhesion Dynamics and Durotaxis in Migrating Cells

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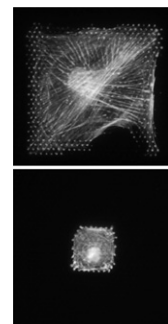
When tissue cells are plated on a flexible substrate, durotaxis, the directed migration of cells towards mechanically stiff regions, has been observed. Environmental mechanical signals are not only important in cell migration, but also seem to influence all aspects of cell differentiation and development, including the metastatic process in cancer cells. Based on a theoretical model suggesting that this mechanosensation has a mechanical basis, we introduce a simple model of a cell by considering the contraction of F-actin bundles containing myosin motors (stress fibers) mediated by the movement of adhesions. We show that, when presented with a linear stiffness gradient, this simple model exhibits durotaxis. Interestingly, since stress-fibers do not form on soft surfaces and since adhesion sliding occurs very slowly on hard surfaces, the model predicts that average cell velocity reaches a maximum at an intermediate stiffness. This prediction could be experimentally tested. We therefore argue that stiffness-dependent cellular adaptations (mechanosensation) and durotaxis are intimately related, and may share a mechanical basis. We therefore identify the essential physical ingredients, which combined with additional biochemical mechanisms, can explain durotaxis and mechanosensation in cells.

1644-Pos Board B554

Cell Shape and Substrate Rigidity Both Regulate Cell Stiffness

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Cells from many tissues sense the stiffness and spatial patterning of their microenvironment to modulate their shape and cortical stiffness. It is still unknown how substrate stiffness, cell shape and cell stiffness modulate or interact with one another. Here, we use microcontact printing and micro-fabricated arrays of elastomeric posts to independently and simultaneously control cell shape and substrate stiffness. Our experiments show that cell cortical stiffness increases both as a function of substrate stiffness and cell shape. When the substrate is very soft, the influence of substrate stiffness is more important than that of cell shape since increasing adherent area does not lead to cell stiffening. On the other hand, when cells are confined to a small area, cell shape effects are more important than substrate stiffness since increasing substrate stiffness no longer affects cell stiffness. These results suggest that both cell size and substrate stiffness can interact in a complex fashion to either enhance or antagonize each other's effect on cell morphology and mechanics.



1645-Pos Board B555

Using Microfluidics to Explore Chemotaxis by the Predatory Bacterium *Bdellovibrio bacteriovorus*

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Bdellovibrio bacteriovorus is a Gram-negative proteobacterium that preys upon a wide variety of other Gram-negative bacteria in the environment. Sensing of and movement toward suitable prey is likely critical to survival of a predator, and indeed, twenty chemotaxis receptors and the associated signaling and flagellar proteins have been discovered in the *Bdellovibrio* genome. Nevertheless, *Bdellovibrio* chemotaxis has never been demonstrated using conventional assays, and the molecules that bind to its chemotaxis receptors have not yet been identified.

We are using microfluidics to explore chemotaxis in individual *Bdellovibrio* predators. Microfluidics focuses on creating devices for controlling fluid at the micrometer scale, where fluid interfaces and concentration gradients can be finely manipulated. In this study, we designed and fabricated a microfluidic device within which gradients of sugars, metabolites, signaling molecules, and other molecules of interest can be established. *Bdellovibrio* predators are introduced to the gradient and are allowed to move in response to the molecules in their environment. Unlike conventional assays