Thursday contributed talks

Ulrich Schwarz

University of Heidelberg
"Emergence of elasticity in cell mechanics"
Biological cells adapt shape and behavior to their mechanical environment through an intricate system of mechanotransduction processes. While in highly dynamic situations like development, cell migration or wound healing, cells need to be soft and viscous, in homeostatic situations like maintenance of connective or epithelial tissues, they have to keep stresses and strains for long times, like an elastic material. Because the actomyosin cytoskeleton determining cell mechanics is in a state of constant turnover, achieving effectively elastic behavior is a real challenge for cells. In this talk, I will first discuss the experimental evidence for the elastic behavior of cells, including the invaginated shapes of single cells in connective tissue and the elastic nature of epithelial monolayers as revealed by traction force and monolayer stress microscopy. I then will discuss different mechanisms which allow this elastic behavior to emerge on cellular scales, including the generation of stress fibers, the exchange dynamics of fast and slow myosin motors in myosin minifilaments and their regulation through the Rho-pathway, which can be controlled e.g. by optogenetics. In each case, I will address the fundamental question how multi-scale modeling and homogenization techniques can be used to mathematically connect the microscopic and macroscopic scales.

Fabian Spill

University of Birmingham
"Role of physical and geometrical drivers of tumour metastasis"
Cancer mostly kills through metastasis - the process where cancer cells leave the primary tumour and colonialize distant organs. Such movement of cells naturally requires forces. How cells generate forces through molecular pathways is thus an intense field of study. Moreover, it is becoming increasingly appreciated that forces, and other physical properties, not only arise from intracellular pathways, but can also reprogram pathways, for instance, through molecular mechanosensors. I will present recent results obtained from mathematical modelling and experimental work aimed at investigating the interplay of physical, geometrical and molecular drivers of tumour progression. At the example of an endothelial cell monolayer, I will show how forces alter the chemical binding rates of cell-cell adhesions, which consequently can lead to gaps in the monolayer. Experiments show that these gaps can be exploited by cancer cells when transmigrating through the endothelial monolayer - a crucial process during metastasis. I will then present some work on modelling mechano-chemical pathways in cells. Pathways including the YAP/TAZ and Rho signalling pathways are sensitive e.g. to extrinsic factors such as extracellular stiffness, or intrinsic factors such as cellular geometry. The complex interplay of such factors can lead to reprogramming of cells. Consequently, a physically altered tumour microenvironment can activate intracellular pathways and, independent or complementary to genetic changes, alter tumour cells towards more aggressive behaviour.

Carina Dunlop

University of Surrey
"Cytoskeletal contractility in mechanosensing"
Cells have been demonstrated to be extremely sensitive to the physical properties of their external environments, changing behaviours as diverse as proliferation, differentiation and migration in response. The mechanism by which this mechanosensing is achieved is broadly understood. Molecular motors em- bedded within the cellular cytoskeletal network bring the network into tension - this contraction is resisted by the cellular adhesion to the external environment with the degree of resistance thus broadly signalling information about the local external stiffness. Great strides have been made in understanding the molec- ular signalling mechanisms mechanisms with research focusing on the focal adhesions, supramolecular adhesive patches, and on pathways such as YAP/TAZ. However, there is emerging evidence of signalling away from focal adhesions including at the nuclear envelope (nuclear mechanotransduction). This necessitates a spatially resolved model of cell stiffness sensing that incorporates intracellular mechani- cal interactions. Here I will present a continuum elasticity model of cellular contractility and stiffness sensing that accounts for the experimentally observed variations in contractile activity within cells. This model demonstrates how on stiff substrates non-uniform contraction will lead to localised regions of internal cell stretch well away from focal adhesions. Additionally where the cell shape is elongated (as is often observed on stiff substrates) this effect is enhanced with increased internal stretch as compared with isotropic cells. These internal strains offer a potential physical mechanism linking physical exter- nal substrate stiffness to stretch activated molecular signalling within the cell and at the nuclear envelope.

Benedikt Sabass

Forschungszentrum Juelich
"Substrate durokinesis of the bacterium P. aeruginosa"
Bacteria can generate mechanical forces that are important for the colonization of surfaces, forma- tion of biofilms, and infection of host cells. In Gram-negative bacterial pathogens, such as Pseudomonas aeruginosa, forces result from ATP-hydrolysis-driven extension-retraction cycles of extracellular filaments called type-IV pili. How bacteria adapt their pilus-based behavior to the mechanical environment is not known. Here, we show that the early stage of surface colonization by P. aeruginosa is modulated by substrate-dependent pilus activity. Our experimental data reveals a complex response of the bacterial migration machinery to substrate properties, including adaptation of the dynamics of pili, their spatial arrangement, and their number. The combination of the experimental data with mathematical modeling allows us to construct a comprehensive picture of the stochastic dynamics of pilus-based motion of P. aeruginosa on different substrates. Overall, our findings reveal how mechanoregulation is involved in essential aspects of the migratory behavior of a paradigmatic bacterial pathogen.