BP 5: Tissue Dynamics & Developmental Processes

Time: Monday 14:00–16:45 Location: ZEU 250

Invited Talk BP 5.1 Mon 14:00 ZEU 250

Are biomechanical changes necessary for tumor progression? - The impact of cell mechanics on cancer development — •Mareike Zink, Anatol Fritsch, Tobias Kiessling, K. David Nnetu, Steve Pawlizak, Franziska Wetzel, and Josef Käs — Abteilung Physik der weichen Materie, Fakultät für Physik und Geowissenschaften, Universität Leipzig, Leipzig, Germany

With an increasing knowledge in tumor biology an overwhelming complexity becomes obvious which roots in the diversity of tumors and their heterogeneous molecular composition. Nevertheless in all solid tumors malignant neoplasia, i.e. uncontrolled growth, invasion of adjacent tissues, and metastasis, occurs. Physics sheds some new light on cancer by approaching this problem from a functional, materials perspective. Recent results indicate that all three pathomechanisms require changes in the active and passive cellular biomechanics. Malignant transformation causes cell softening for small deformations which correlates with an increased rate of proliferation and faster cell migration. The tumor cell's ability to strain harden permits tumor growth against a rigid tissue environment. A highly mechanosensitive, enhanced cell contractility is a prerequisite that tumor cells can cross its tumor boundaries and that this cells can migrate through the extracellular matrix. Insights into the biomechanical changes during tumor progression may lead to selective treatments by altering cell mechanics. Such drugs would not cure by killing cancer cells, but slow down tumor progression with only mild side effects and thus may be an option for older and frail patients.

BP 5.2 Mon 14:30 ZEU 250

Blood flow and blood cell interactions and migration in microvessels — •Dmitry Fedosov, Julia Fornleitner, and Gerhard Gompper — Forschungszentrum Juelich, Institute of Solid State Research, Juelich 52425, Germany

Blood flow in microcirculation plays a fundamental role in a wide range of physiological processes and pathologies in the organism. To understand and, if necessary, manipulate the course of these processes it is essential to investigate blood flow under realistic conditions including deformability of blood cells, their interactions, and behavior in the complex microvascular network which is characteristic for the microcirculation. We employ the Dissipative Particle Dynamics method to model blood as a suspension of deformable cells represented by a viscoelastic spring-network which incorporates appropriate mechanical and rheological cell-membrane properties. Blood flow is investigated in idealized geometries. In particular, migration of blood cells and their distribution in blood flow are studied with respect to various conditions such as hematocrit, flow rate, red blood cell aggregation. Physical mechanisms which govern cell migration in microcirculation and, in particular, margination of white blood cells towards the vessel wall, will be discussed. In addition, we characterize blood flow dynamics and quantify hemodynamic resistance.

BP 5.3 Mon 14:45 ZEU 250

Cell flow reorients planar cell polarity in the developing wing epithelium of the fly — •Douglas B. Staple[1], Reza Farhadifar[1], Benoît Aigouy[2], Andreas Sagner[2], Jens-Christian Röper[2], Suzanne Eaton[2], and Frank Jülicher[1] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

Epithelia are two-dimensional sheets of cells. Cell polarity in epithelia typically forms large scale aligned patterns in the plane of the tissue. In the *Drosophila* wing, an important model system for the study of epithelial organization, this planar polarity is reflected in the pattern of wing-hairs and in the distribution of planar cell polarity (PCP) proteins at earlier stages during development. Here we investigate the mechanisms underlying the dynamic reorganization of planar cell polarity in the *Drosophila* wing using a combination of theory and experiment. Experimentally, we perform time-lapsed imaging during pupal development in order to extract both the time-dependent distribution of PCP proteins, and also the spatially and temporally inhomogeneous cell flow field in the tissue. The pattern of PCP proteins is found to reorient during development. We decompose the velocity field into patterns of local shear, compression, and rotation rates. Given the time-dependent shear and rotation rates and an experimentally measured initial condition, the time-evolution of the polarity pattern is computed using a phenomenological hydrodynamic theory, and is found to be consistent with the experimentally observed time-evolution.

BP 5.4 Mon 15:00 ZEU 250

Fluidization of tissues due to cell division and apoptosis — •Jonas Ranft[1,2], Markus Basan[1], Jens Elgeti[1], Jean-François Joanny[1], Jacques Prost[3], and Frank Jülicher[2] — [1]Institut Curie, 26 rue d'Ulm, 75005 Paris, France — [2]Max-Planck-Institut für Physik komplexer Systeme, Nöthnitzer Str. 38, 01187 Dresden, Germany — [3]ESPCI, 10 rue Vauquelin, 75005 Paris, France

Throughout development, tissues grow due to continuous cell division. In later stages, tissues can reach a homeostatic state in which cell division and cell death balance on average. In addition to genetic regulation, the mechanics of tissues play an important role in these processes. We develop a continuum description of tissue dynamics in order to account for the stress distribution and cell flows on large scales [1]. In the absence of cell division and apoptosis, we consider the tissue to behave as an elastic solid. Cell division and apoptosis introduce stress sources which in general are anisotropic. By combining cell number balance with dynamic equations for the stress source, we show that the tissue effectively behaves as a visco-elastic fluid with a relaxation time set by the rates of division and apoptosis. We find that close to the homeostatic state, the compressional modulus of the tissue vanishes on long time scales. We discuss the effects of fluctuations in cell division and apoptosis and compare our results to simulations of multicellular systems. This approach can be extended to a two-component description of tissues that takes the extracellular fluid explicitly into account.

[1] Ranft et al., PNAS, 2010 Nov 15. (Epub ahead of print)

BP 5.5 Mon 15:15 ZEU 250

Pattern formation in active fluids — •Justin Bois[1,2], Frank Jülicher[1], and Stephan Grill[1,2] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

We discuss pattern formation in active fluids in which active stress is regulated by diffusing molecular components. Nonhomogeneous active stress profiles create patterns of flow which transport stress regulators by advection. Our work is motivated by the dynamics of the actomyosin cell cortex in which biochemical pathways regulate active stress. We present a mechanism in which a single diffusing species up-regulates active stress, resulting in steady flow and concentration patterns. We also discuss general pattern-formation behaviors of reaction diffusion systems placed in active fluids.

15 min. break.

BP 5.6 Mon 15:45 ZEU 250

General analysis of mathematical models for bone remodeling — •Martin Zumsande[1], Dirk Stiefs[1], Stefan Siegmund[2], and Thilo Gross[1] — [1]Max Planck Institute for the Physics of Complex Systems, 01187 Dresden, Germany. — [2]Department of Mathematics, Dresden University of Technology, 01062 Dresden, Germany.

Bone remodeling is a complex process by which the skeleton of vertebrates is rebuilt continuously throughout their life. It is based on the interplay of two cell types, bone-resorbing osteoclasts and bone-forming osteoblasts and regulated by various cytokines, hormones and other signaling agents. In this work, we apply the method of generalized modelling to systematically analyse a large class of mathematical models of bone remodeling that are based on ODEs. Our analysis shows that the precursors of osteoblast play an important role in the regulation of bone remodeling. Further, we find that stability of the steady state, which is required in the physiological state, is not a self-evident properties of the models. In contrast, the parameter regime that is most likely realized in nature based on experimental input is situated close to bifurcation lines, marking qualitative changes in the dynamics. Although proximity to a bifurcation facilitates adaptive responses to changing external conditions, it entails the danger of losing dynamical stability. These dynamical transitions can possibly be related to diseases of bone such as Paget's disease.

BP 5.7 Mon 16:00 ZEU 250

Oct4 kinetics predicts cell lineage patterning in the early mammalian embryo — Nicolas Plachta[1], •Tobias Bollenbach[2,3], Shirley Pease[1], Scott E. Fraser[1], and Periklis Pantazis[1] — [1]California Institute of Technology, Pasadena, CA, USA — [2]Harvard Medical School, Boston, MA, USA — [3]IST Austria, Klosterneuburg, Austria

Transcription factors (TFs) are central to sustaining pluripotency in mammalian development. Here, we establish a fluorescence decay after photoactivation (FDAP) assay to quantitatively study the nuclear transport kinetics of Oct4, a key TF controlling pre-implantation development in the mouse embryo. Combining FDAP measurements with a physical description of nuclear transport, we reveal that each cell in a developing mouse embryo exhibits one of two distinct Oct4 kinetic profiles, before there are any morphologically distinguishable differences or outwards signs of lineage patterning. By tracing the lineages of the cells in these two distinct sub-populations, we find that Oct4 kinetics predicts lineages of the early embryo. Cells in which FDAP reveals slower Oct4 kinetics are much more likely to contribute to the pluripotent cell lineage which creates the inner cell mass and later gives rise to the fetus. In contrast, cells with faster Oct4 kinetics contribute almost exclusively to the extra-embryonic lineages which later form the placenta. Our findings identify Oct4 nuclear transport kinetics, rather than differences in total expression levels, as a predictive measure of cell lineage patterning in the early mouse embryo.

Reference: N. Plachta et al., Nature Cell Biology, accepted.

BP 5.8 Mon 16:15 ZEU 250

Mechanotaxis in the brain — •Kristian Franze[1,2], Hanno Svoboda[2], Pouria Moshayedi[1,3], Andreas Christ[1], James Fawcett[3], Christine Holt[2], and Jochen Guck[1] — [1]Department of Physics — [2]Department of Physiology, Development and Neuroscience — [3]Brain Repair Centre, University of Cambridge, UK

Biophysics is just beginning to unravel important physical problems in biology and medicine that have been mostly overlooked for decades. While neuroscience has mainly focused on biochemical and molecular biological aspects of neuronal migration and growth, virtually nothing is known about mechanical aspects. Here we show that both neurons and glial cells, the basic building blocks of nerve tissue, respond to mechanical stimuli in their environment. Mechanosensing involves the application of forces driven by the interaction of actin and myosin II, and intracellular calcium signaling. Using culture substrates incorporating gradients of mechanical properties, we found that neuronal axons are repelled by stiff substrates while activated glial cells are attracted toward them. Applying a modified scanning force microscopy technique, we found mechanical gradients in nerve tissue along which neurons grow *in vivo*. Hence, our data suggest that cell growth and migration in the central nervous system are not only guided by chemical signals - as it is currently assumed - but also by the nerve tissue's mechanical properties.

BP 5.9 Mon 16:30 ZEU 250

Dynamics of asexual reproduction in planarians — Bryan Lincoln, Sofia Quinodoz, and •Eva-Maria Schoetz — 170 Carl-Icahn Laboratory, Princeton University, Princeton, NJ, USA

Planaria research has undergone a recent resurgence due to the development of molecular tools, the Planarian genome project and database resources. Despite the resulting progress in planarian biology research, an extensive study of their physical properties remains to be undertaken. We have developed a method to collect a large amount of data on the dynamics of clonal reproduction in the freshwater planarian S.mediterranea. The capability of planarians to regenerate from a minuscule body part on the order of 10000 cells is based on a homogeneously distributed stem cell population that comprises ~30% of all cells. Due to this stem cell contingent, planarians can further reproduce spontaneously by dividing into a larger head and smaller tail piece, which then will rebuild the missing body parts, including a central nervous system, within about a week. Time-lapse imaging allows us to characterize the fission process in detail, revealing its developmental stages and capturing the critical moment of rupture. A traction force measurement setup is being developed to allow us to quantify the forces planarians exert on the substrate during reproduction, a macroscopic analog to the Traction Force Microscopy setups used to determine local cellular forces. We are particularly interested in the molecular processes during division and the interplay between tissue mechanics and cell signaling.