BP 15: Posters: Multi-cellular systems

Time: Monday 17:30–19:30 Location: Poster A

BP 15.1 Mon 17:30 Poster A

GPU accelerated simulation of light propagation through retinal volumes mapped by multi-photon microscopy — •Martin Weigert, Alfonso Garcia-Ulloa, Heike Petzold, Kaushikaram Subramanian, Eugene Myers, and Moritz Kreysing — Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

The architecture of photoreceptor cells (PRC) nuclei differs considerably between nocturnal and diurnal mammals: whereas diurnal mammals possess conventional PRC nuclei, nocturnal mammals show a uniquely inverted PCR architecture characterized by the compaction of dense heterochromatin in the nuclear center. As the refractive index increases with molecular density, this nuclear inversion was suggested to reduce light scattering as inferred by 2D simulation, and direct measurement on individual isolated nuclei.

Here we show how a beam propagation method implemented on GPU accelerators can considerably speed up these calculations and allows for simulating the propagation of light through realistically large 3D retinal volumes. This way we studied the evolution of the angular spectrum of light on its way through a 3D model of the outer nuclear layer, which we obtained from multi-photon microscopy. We found that the near field coupling between cell nuclei of inverted architecture leads indeed to an overall reduction in scattering, as opposed to an absolute summation of the individual cell scattering contributions.

BP 15.2 Mon 17:30 Poster A

Osmolarity mediated growth of MDCK model tissue — •Damir Vurnek[1], Sara Kaliman[1], Carina Wollnik[2], Florian Rehfeldt[2], and Ana-Sunčana Smith[1] — [1]Theoretical Physics I, FAU Erlangen — [2]3rd institute Phyiscs-Biophysics, Georg-August University, Göttingen

The capacity to adapt to changes in environmental osmotic conditions is vital for the functioning of epithelium. We study this response by growing MDCK II model tissues, mm^2 to cm^2 sized clusters, with increased concentrations of mannitol, urea or NaCl. The phase space of tissue viability is characterized from isotonic to elevated toxic conditions. In young colonies, elevated osmotic conditions suppress the growth. With increasing age, adaptation takes place, and the colony develops the same morphology as the controls, with the edge at low and the center at relatively high densities. We characterize the osmolyte/concentration specific proliferation rates, absolute colony sizes, as well as the steady state cell densities. Finally, the internal structure of the cells within the colony is addressed. Even in the intermediate stages of growth DNA damage is evident on the nuclei near the colony edge, however it lacks in the dense bulk of the tissue. Here, two factors could be intertwined. With densification, decreasing apical and basal surfaces expose less cell membrane to the hostile surrounding and/or the proliferating edge is more prone to damage during the cell cycle. As tissue reaches adaptation, high osmolarity brings added features to tissue cooperativity and nuclei elongations show differences in the stress forces for different applied osmolytes.

BP 15.3 Mon 17:30 Poster A

Transporting Dpp in the fly wing: A theoretical analysis. — •Daniel Aguilar-Hidalgo[1], Maria Romanova-Michailidi[2], Marcos González-Gaitán[2], and Frank Jülicher[1] — [1]Max Panck Institute for the Physics of Complex Systems, Dresden, Germany — [2]University of Geneva, Department of Biochemistry, Sciences II, Quai Ernest-Ansermet 30 1211, Geneva 4, Switzerland

Morphogens are signaling molecules, which are locally secreted and spread in a tissue, where they form graded concentration profiles. Such profiles can provide positional information to the tissue cells, or can act as growth factors stimulating cell and tissue growth. The mechanisms by which morphogens are transported in a tissue are still a matter of debate. We study the dynamics of the morphogen *Decapentaplegic* (Dpp) in the developing fly wing. Dpp is secreted from a stripe of cells situated at the anterior-posterior compartment boundary of the wing imaginal disc, and spreads to both anterior and posterior targets. We analyze the dynamical properties of two proposed transport mechanisms for Dpp in the wing: (i) a model of effective diffusion by trancytocis and (ii) a model of free diffusion with internalization. This analysis reveals key dynamical differences if endocytosis is perturbed. This could allow distinguishing possible transport mechanisms in experiments using fluorescence recovery after photobleaching (FRAP) techniques and temperature sensitive dynamics mutants.

BP 15.4 Mon 17:30 Poster A

Diffusion and bulk flow in phloem loading - a theoretical study of the polymer trap mechanism in plants — •Hanna Rademaker[1], Julia Dölger[1,3], Johannes Liesche[2], Alexander Schulz[2], and Tomas Bohr[1] — [1]Technical University of Denmark — [2]University of Copenhagen, Denmark — [3]Technische Universität Darmstadt, Germany

Plants photosynthesize sugars for storage and growth inside the mesophyll cells of their leaves. In order to distribute them, the sugars are *loaded* into the *phloem* vascular system. The osmotic uptake of water increases the pressure in the phloem cells, which then drives the bulk flow throughout the plant, according to the "Münch mechanism" (1930). We studied one special loading mechanism, the so-called "polymer trap", in which sucrose is believed to diffuse from the mesophyll into the phloem via small symplasmic channels, called *plasmodesmata* (PDs). Sucrose is then partly converted into larger sugar molecules, which are unable to diffuse back through the narrow PDs. One major concern about this hypothesis was, if sucrose was still able to be transported in sufficient quantity, while molecules less than 20% larger should be completely blocked. Our theoretical study [Dölger et al., Physical Review E **90**, 042704, (2014)] shows, that the polymer trap mechanism can in principle function, and that not only diffusion, but also bulk flow, could be involved in the loading mechanism itself, making it more efficient. We are now focusing on experiments, both in plants and in microfluidic devices, testing our theoretical predictions about the symplasmic uptake of water into the phloem.

BP 15.5 Mon 17:30 Poster A

Mechanics of Zebrafish doming — •Martin Bock[1], Hitoshi Morita[2], Carl-Philipp Heisenberg[2], and Guillaume Salbreux[1] — [1]MPI-PKS, Dresden, Germany — [2]ISTA, Klosterneuburg, Austria

On the timescale of embryo development, cell rearrangements can allow for stress relaxation so that the tissue may behave as a fluid-like material. Accordingly, surface tensions and tissue flow are essential to establish the shape of organisms. Here we ask how flows during Zebrafish dome formation can be understood quantitatively by describing embryonic tissues as a fluid, active material.

In early Zebrafish morphogenesis, approximately 25% of the embryo volume is occupied by the blastoderm, a 3D sheet of cells, while the remaining 75% comprise the nourishing, bag-like yolk. The two of them juxtapose in such a way that the overall embryo shape is approximately spherical. During the subsequent doming process, the blastoderm thins and starts to spread over the yolk, whereas the yolk bulges upwards into the blastoderm, in a characteristic dome-like shape.

In my presentation, I will describe a physical model of dome formation incorporating surface tensions and bulk stresses, and compare our predictions to experimental data on wildtype embryos and mutants with partially defective doming.

BP 15.6 Mon 17:30 Poster A

Analyzing cellular arrangements and shapes in *Caenorhabditis elegans* — •Rolf Fickentscher, Philipp Struntz, and Matthias Weiss — Experimentalphysik 1, Universität Bayreuth

Recent developments in lightsheet fluorescence microscopy enable rapid and gentle *in toto* imaging of living specimen. Three-dimensional image series with a high spatiotemporal resolution can be acquired over extended periods of time. We utilize these advantages to investigate mechanical cues in the early embryogenesis of the small nematode *Caenorhabditis elegans* by imaging embryos with fluorescently labeled nuclei or plasma membranes [1]. Tracking nuclei yields information about processes that drive cellular arrangements during early development, whereas the segmentation of whole cells provides additional knowledge on shape controlling mechanisms throughout the cell cycle.

We have compared nuclei trajectories in different embryos. The observed deviations are small, hence indicating a robust cellular arrangement process. A simple mechanical model reveals that early cell organization is crucially determined by the cells' quest for a position with least repulsive interactions. This passive process is superimposed

by active shape control, i.e. cell rounding can be observed for all cells at the onset of mitosis. Furthermore, we show that incomplete rounding correlates with the orientation of cell division axes.

[1] R. Fickentscher, P. Struntz & M. Weiss, Biophys. J, 105 (2013)

BP 15.7 Mon 17:30 Poster A

Growth Dynamics of MDCK II Clusters on Elastic Substrates — •Philipp Linke[1], Carina Wollnik[1], Sara Kaliman[2], Damir Vurnek[2], Ana-Sunčana Smith[2], and Florian Rehfeldt[1] — [1]Third Institute of Physics - Biophysics, Georg-August-University, Göttingen, Germany — [2]Institute for Theoretical Physics and Cluster of Excellence: Engineering of Advanced Materials, University Erlangen-Nürnberg, Germany

Cellular motility is an important factor in many processes like wound healing, tissue formation, and immune reactions. Cells adhere to their environment using focal adhesions and react to the stiffness of their surroundings. To study the response of a distinct cell type to different stiffness we use collagen-I coated polyacrylamide (PA) gels with well-controlled stiffness to mimic different environments.

MDCK II cells have proven to be very useful as model system for endothelial morphogenesis. When growing on a flat surface, these cells form a cluster monolayer after a short time. We found in our studies that clusters show a different growth behavior when cultured on PA gels with varied stiffness. The formation dynamics of these structures is controlled by cellular contractility and the balance of cell-cell and cell-matrix contacts. To create wound healing essays we seed the cells in culture inserts from ibidi, which are placed directly onto the collagen coated gels. We are using the open source software Micro Manager in combination with a motorized xy-stage and a heating and CO2 incubation system to do parallel live cell microscopy of several clusters in statistically equivalent, physiological conditions.

BP 15.8 Mon 17:30 Poster A

SPIM applications in organismal biology — •Philipp Struntz, Rolf Fickentscher, and Matthias Weiss — Experimental Physics I, University of Bayreuth, Bayreuth, Germany

Fluorescence imaging is the method of choice when aiming at monitoring dynamic phenomena during embryogenesis. Yet, standard techniques like confocal imaging suffer from inducing a considerable amount of photobleaching and phototoxicity which hampers long-term observations. We have designed and constructed a fully automated single-plane illumination microscope (SPIM) for imaging embryos of the nematode Caenorhabditis elegans in the early stages of development [1]. The combination of rapid widefield detection with optical sectioning and reduced bleaching allows for long-term, three-dimensional imaging of living specimen with a high spatio-temporal resolution. Using our SPIM setup, we have quantified cell movement and arrangment during early embryogenesis. Moreover, we have performed fluorescence correlation spectroscopy measurements (SPIM-FCS) on zygotes of C. elegans that expressed GFP-tagged PIE-1 and PLCdelta1. While the former reports on local diffusion properties during a vital protein condensation phenomenon, the latter series of experiments has probed the diffusional mobility of a vital peripheral membrane protein. Our data show that SPIM provides a versatile tool to explore embryogenetic events on several length scales, i.e. it is hence well suited to examine dynamic pattern formation in organismal biology.

[1] R. Fickentscher, P. Struntz & M. Weiss, Biophys. J. 105, 1805 (2013)

BP 15.9 Mon 17:30 Poster A

A computational model of tumor growth based on large scale vascular networks — Michael Welter[1], •Thierry Fredrich[1], Heiko Rieger[1], and Herbert Rinneberg[2] — [1]Saarland University — [2]PTB Berlin

The process of tumor growth is very complex. Even today it is hard to predict the outcome of the disease and the effect of various therapies. Theoretical simulations can help to make such predictions and allow tailoring the therapy to patient specific microenvironments such as the blood vessel network.

On the way there, we consider the creation of a healthy host vessel system by stochastic growth of a hierarchical arteriovenous network (described in [1]) as starting point. Parameters can be adjusted to yield networks with global properties like MVD, vascular volume and perfusion, which agree very well with data from real tissue. We treat the bulk of tumor cells with a continuum approach following [2] and consider vessels as linelike sources or sinks for nutrients, coupled to the tissue layer via some transvascular flux.

Interstitial fluid flow, for example, is a key element of chemotherapy, however not yet fully understood. The locally available nutrients play another important role in cancer proliferation. We investigate those aspects using a model [3] inspired by morphological data from human melanoma and breast tumors. We were able to quantitatively reproduce IR mammography data [4] showing the oxygen content of breast carcinomas in vivo.

[1] Gödde and Kurz, [2] Preziosi, [3] Welter and Rieger, [4] Rinneberg

BP 15.10 Mon 17:30 Poster A

Mechanistic models of carcinogenesis: Radiation-induced risk of lung cancer in the Mayak workers — •Sascha Zöllner[1], Mikhail Sokolnikov[2], and Markus Eidemüller[1] — [1]Helmholtz Zentrum München, Institute of Radiation Protection (Germany) — [2]Southern Urals Biophysics Institute, Ozyorsk (Russia)

Mechanistic multi-stage models are used to analyze lung-cancer mortality after Plutonium exposure in the Mayak-workers cohort. Besides the established two-stage model with clonal expansion, models with three mutation stages as well as a model with two distinct pathways to cancer are studied. The results suggest that three-stage models offer an improved description of the data. The best-fitting models point to a mechanism where radiation increases the rate of clonal expansion. This is interpreted in terms of changes in cell-cycle control mediated by bystander signaling or repopulation following cell killing. To elucidate the implications of the different models for radiation risk, several exposure scenarios are studied. Models with a radiation effect at an early stage show a delayed response and a pronounced drop-off with older ages at exposure. Moreover, the dose-response relationship is strongly nonlinear, revealing a marked increase above a critical dose.

BP 15.11 Mon 17:30 Poster A

Investigating the influence of Keratin/Vimentin on the invasive behavior of epithelial cells — •Paul Heine and Josef Käs — Soft Matter Physics (PMW), Leipzig University, Germany

During tumor development epithelial cells undergo a remarkable carcinogenetic transition to a mesenchymal phenotype. This Epithelial-Mesenchymal Transition (EMT) facilitates a variety of mechanical and biochemical changes within the affected cells which produces drastic changes in their cell polarity, cell-cell adhesion, migratory and invasive properties. Some of the key components of this conversion were identified to be the intermediate filaments Keratin and Vimentin. While the remodeling of these cytoskeletal components has been partially understood, their complex relationship has not been thoroughly investigated. We aim to classify the significance of Vimentin as a counteracting factor to Keratin in the invasiveness and metastatic potential. An investigation of the migratory, proliferative and invasive behavior of epithelial cells in constricting channels and with a variety of modulations to their intermediate filament cytoskeleton should produce vital insights for understanding metastatic initiation.

BP 15.12 Mon 17:30 Poster A

Glassy Dynamics in a Receptor Dynamics Model for Tumorigenesis — •Yuting Lou and Yu Chen — SCS Lab, Department of Human and Environmental Engineering, Graduate School of Frontier Science,University of Tokyo, Tokyo, Japan

A multi-cell receptor dynamics model for tumorigenesis is built for investigating the diversity of homeostasis and the origin of abnormal preneoplastic dynamics from a systematical perspective. Our simulations of cells growth and wound healing show the homeostasis state presents rich glassy dynamics such as diverse relaxation patterns from a wound perturbation, a large spectrum of relaxation timescale for reaching cell arrest, aging, and ergodicity breaking.The origin of the homeostatic diversity lies in these glassy dynamics whose characteristic timescales differs. Several parameters have been studied and the ability of cell arrest was found to be the role of control factor deciding the scale of the process. The size scale of the cell mass increase with the time scale of relaxation within which all cells reach its arrest state.Another simulation with the mechanism of genetic deficiency newly added to the receptor dynamics model, found that mutations help extend this scale in a normal homeostatic process.This dependency helps render a hypothesis: cancer happens when the system is undergoing glass transition where the relaxation time goes to infinity in terms of our observation timescale. This draw a unified picture for the initiation of benign tumor and cancer, and also explains the reason why these diseases feature long latency before exploding as well as the large spectrum of periods before they relapse.