BP 26: Multi-cellular systems and Physics of Cancer

Time: Wednesday 11:45–13:30 Location: ZEU 250

BP 26.1 Wed 11:45 ZEU 250

Modeling the electrical excitation in a cross section of the human heart with simultaneous consideration of varied cell-type distribution, fiber-angle rotation and stimulation protocol. — •Maximilian Eisbach[1], Stefan Fruhner[2], Harald Engel[1], and Markus Bär[2] — [1]TU Berlin — [2]PTB Berlin

The anisotropy of the electrical conduction system in a human heart is believed to play a critical role in the electrical wavefront dynamics. Yet, the validity of rule based approaches for embedding fibre orientation and cell-type distribution remains unclear. We investigated the influence of different fibre assignments and cell type distribution on the propagation of the electrical excitation in a 2D slice obtained from MRI measurements of a human heart. Since a cross section is a radical simplification of the 3D structure of the human heart, we additionally studied the impact of varying stimulation protocols. We conclude that the stimulation position has a greater influence on the shape of the excitation wave in a cross section of the heart, than differing anisotropy of the electrical conduction system.

BP 26.2 Wed 12:00 ZEU 250

Osmotic effects in MDCK model tissues — •Damir Vurnek[1], Sara Kaliman[1], Matthias Gebhardt[2], Florian Rehfeldt[3], Katrina Binger[2], and Ana-Sunčana Smith[1] — [1]Institut für Theoretische Physik, Universität Erlangen-Nürnberg — [2]Max-Delbrück Center for Molecular Medicine, Berlin — [3]3^{rd} Institute of Physics-Biophysics, University of Göttingen

The capacity to respond and adapt to changes in the environmental osmotic conditions is vitally important for the functioning of epithelial tissues. We study this response by growing MDCK II model tissues in environments with an increased concentration of mannitol, urea or NaCl. The phase space of tissue viability is established and characterized from isotonic to elevated toxic conditions. Furthermore, we identify the time scales on which the survival, growth and the internal organization of the colony is affected. In young colonies, elevated osmotic conditions suppress the growth. As the age of the colony increases, adaptation takes place, and the colony develops the same morphology as the controls, with the edge at the low and the center at relatively high densities. We show that the appearance of this internal organization is independent of the initial configuration of seeded cells. Apart from the general trends, example of which is the quadratic growth of the area observed in the young colonies, we characterize the osmolyte-and concentration-specific proliferation rates, growth rates and absolute colony sizes, as well as the steady state cell densities. Finally, we analyze the internal structure of cells within the colony and characterize the changes in their nuclei shape and the evident DNA damage.

BP 26.3 Wed 12:15 ZEU 250

Size control on the fly ocellar complex pattern — •Daniel Aguilar-Hidalgo[1], David Becerra-Alonso[2], María Carmen Lemos[3], Antonio Córdoba[3], and Fernando Casares[4] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany. — [2]Dept. Engineering and Mathematics - Univ. Loyola Andalucía, Sevilla, Spain. — [3]Dept. Condense Matter Physics - Univ. de Sevilla, Sevilla, Spain. — [4]CABD (CSIC-UPO), Sevilla, Spain.

During development, organs grow until reaching a specific size. Different species show distinct organ sizes maintaining functionality. We are studying the organ growth scalability in the *D. melanogaster* ocellar complex. It comprises three simple eyes, or ocelli, located at the vertices of a triangular patch of cuticle on the fly's forehead. This pattern sets the specification of two mutually alternative cell fates: (1) interocellar cuticle flanked by two (2) ocelli. We developed a mathematical and computational model as a gene regulatory network (GRN) that describe the qualitative aspects of the patterning and predicts several of its properties [1]. In nature, different fly species show different size distribution of the ocellar complex constituents. Is the same GRN able to generate different size distributions? We found that randomized parametric sets show not random but structured size distributions. A study of this distribution on several fly species show the same structure as predicted by the model. This suggests that the same GRN defines different sizes for the ocellar complex, and that the system constrains the possible distribution results, avoiding non-functional structures.

[1] Aguilar-Hidalgo *et al.* Development, (2013) 140 (1), 82-92.

BP 26.4 Wed 12:30 ZEU 250

Physical Principles of Body Plan Scaling in Planarians — •Steffen Werner[1], Manuel Beirán Amigo[1], Jochen Rink[2], Frank Jülicher[1], and Benjamin M. Friedrich[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

In many biological systems, body plan patterning operates at variable length scales during development and regeneration. The flatworm Planarian is a master of regeneration and body plan scaling, inspiring our theoretical work on fundamental principles of scalable pattern formation.

Planarians can grow and actively degrow by more than an order of magnitude in size, depending on feeding conditions, while maintaining shape and function of all parts of the body. Moreover, Planarians can rebuild its entire body plan from a tiny amputation fragment, prompting for size-independent mechanisms of self-organized body patterning.

We are interested in general principles underlying scalable pattern formation that go beyond classical Turing mechanisms. Turing mechanisms provide a means of self-organized patterning that is characterized by an intrinsic length scale, which eventually precludes scaling. We discuss feedback mechanisms that adjust this length-scale to the system size in an autonomous manner, resulting in a minimal model for robust pattern-formation that scales with system size. We are closely collaborating with the experimental lab of Jochen Rink at the MPI CBG (Dresden) to apply our theoretical framework to Planarians.

BP 26.5 Wed 12:45 ZEU 250

A Distinct Intermolecular FasL Distance Triggers Either Apoptosis or Proliferation in Glioma and Pancreatic Cancer Cells — •Cornelia Monzel[1], Thomas Kaindl[1], Joel Beaudouin[2,3], Susanne Kleber[2], Marcin Teodorczyk[2,4], Motomu Tanaka[1,5], and Ana Martin-Villalba[2] — [1]Dept. of Physical Chemistry of Biosystems, Heidelberg University, Germany — [2]Dept. of Molecular Neurobiology, DKFZ, Heidelberg, Germany — [3]Dept. of Signal Transduction Biophysics, BioQuant, Heidelberg, Germany — [4]Inst. for Microscopic Anatomy and Neurobiology, Mainz University, Germany — [5]Inst. for Integrated Cell Materials Science, Kyoto University, Japan

The trimerized Fas receptor-ligand (Fas-FasL) interaction has long been described as inducer of apoptosis, but recent studies also suggest its critical role in proliferation or metastasis. In order to elucidate the mechanisms inducing cell death we designed quantitative cell surface models of supported lipid membranes displaying FasL at defined intermolecular distances (6-17 nm). Utilizing live cell imaging, we evaluated the reaction kinetics of cancer apoptosis. Intriguingly, in both glioma and pancreatic cancers an optimal ligand distance for the most effective apoptosis was found, which was accompanied by increased Fas-FasL aggregate formation. In contrast, when we transferred this membrane on microbeads injected into 3D tumors, pronounced proliferation and self-renewal in vivo and in vitro was observed. These findings demonstrate the significant impact of a distinct FasL distance, which results in opposite consequences in single- and multicellular sytems.

BP 26.6 Wed 13:00 ZEU 250

Multiple mutations in hierarchically organized tissues. — •Benjamin Werner[1], David Dingli[2], and Arne Traulsen[1] — [1]Max Planck Institute for Evolutionary Biology, Plön Germany — [2]Mayo Clinic, Rochester USA

Cancers are rarely caused by single mutations, but often develop based on the combined effects of multiple mutations. For most cells, the number of possible cell divisions is limited due to various biological constrains, as for example progressive telomere shortening or a hierarchically organized tissue structure. Thus, the risk of accumulating cells carrying multiple mutations is low. Nonetheless, many diseases are based on the accumulation of such multiple mutations. We model a general, hierarchically organized tissue by a multi compartment approach, allowing any number of mutations within a cell. I present closed solutions for the deterministic clonal dynamics and the reproductive capacity of single clones. I show that hierarchically organized

tissues strongly suppress cells carrying multiple mutations and derive closed solutions for the expected size and diversity of clonal populations founded by a single mutant within the hierarchy.

References:

Werner B., Dingli D., Lenaerts T., Pacheco J. M., and Traulsen A. Dynamics of mutant cells in hierarchical organized tissues. PLoS Computational Biology 2011(e1002290)

Werner B., Dingli D. and Traulsen A. A deterministic model for the occurrence and dynamics of multiple mutations in hierarchically organized tissues. Journal of the Royal Society Interface 2013 (10)

BP 26.7 Wed 13:15 ZEU 250

Computer Simulation of the Metastatic Progression and Treatment Interventions — •Anja Bethge[1], Udo Schumacher[2], and Gero Wedemann[1] — [1]CC Bioinformatics, University of Applied Sciences Stralsund, Germany — [2]Institute for Anatomy and Experimental Morphology, University Medical Center Hamburg-Eppendorf, Germany

The process of metastasis formation is still subject of discussion and even established models differ considerably in several basic details and conclusions drawn from them. A computer model was developed which permits comparison of different models quantitatively with clinical data and which additionally predicts the outcome of treatment interventions. It is based on a discrete event simulation protocol. The growth of the primary tumour is described via analytical functions, while a rate function models the intravasation events of the primary tumour and its metastases. Events describe the behaviour of the emitted malignant cells until the formation of new metastases. Using the computer model we investigated different questions: Are metastases able to metastasize? Is metastasis an early or a late event? Do metastases undergo a dormancy phase before they start to grow out into a macro metastasis? (Bethge et al. PLoS ONE 7(4): e35689, 2012) We studied the effects of different treatments, such as the resection of the primary tumour, radionuclide therapy, radioembolization and chemotherapy in the model.