BP 19: Multi-cellular systems

Time: Tuesday 9:30–12:45 Location: H 1058

Invited Talk BP 19.1 Tue 9:30 H 1058

Emerging social behaviour during aggregation in Dictyostelium discoideum — Giovanna De Palo[1], Darvin Yi[2], Thomas Gregor[2], and •Robert Endres[1] — [1]Department of Life Sciences, Imperial College London, UK — [2]Joseph Henry Lab. of Physics, Princeton University, USA

During starvation, the social amoeba Dictyostelium discoideum aggregates artfully via pattern formation into a multicellular slug and finally spores. The aggregation process is mediated by the secretion and sensing of cyclic adenosine monophosphate (cAMP), leading to the synchronised movement of cells. The whole process is a remarkable example of collective behaviour, spontaneously emerging from single-cell chemotaxis. Despite this phenomenon being broadly studied, the precise mechanism of aggregation starting from single cells is still unclear. Here, we extend a detailed single-cell model of D. discoideum chemotaxis by adding cell-cell communication. We then use these results to build a population model with rules derived from single cells. We validate our results with experimental FRET data, where both intracellular concentration of cAMP and collective movements are measured. By analysing cell shape and behaviour we show evidence of a critical point at the onset of aggregation. Specifically, by considering the morphospace we show how the average cell shape changes with the directional correlation diverging exactly during the streaming process. Similar methods could also be exploited for the understanding of other examples of collective behaviours, ranging from the complexity of animal migration to cell organisation in embryonic morphogenesis.

BP 19.2 Tue 10:00 H 1058

Adaption of fluid flow in the slime mold *Physarum polycephalum* — •Karen Alim, Gabriel Amselem, François Peaudecerf, Anne Pringle, and Michael Brenner — Harvard University, Cambridge, U.S.A.

The network-forming slime mold *Physarum polycephalum* lacks any central coordination center, yet it shows often-termed intelligent dynamics in the way it grows and adapts its network morphology. Our work investigates the role of fluid mechanics for transport and signal transfer during the morphological dynamics of this network-like slime mold. We combine experimental observations of the fluid flow and its driving force with the development of the theoretical concept of transport by peristaltic flow in a network. This synergy allows us to show that the slime mold actively controls its internal fluid flow by establishing a peristaltic wave. This peristaltic wave always spans the total extent of an individual independent of its size. Thus, we find that the slime mold actively adapts its flows as to maximize transport. The quantitative description of flows in *P. polycephalum* enables a new view on the slime molds growth dynamics during the encounter of food or toxins and how their location can be 'remembered', an important step to perform an informed decision during an individuals network growth and adaptation.

BP 19.3 Tue 10:15 H 1058

Foraging in the Slime Mold Physarum polycephalum — •Jonghyun Lee, Christina Oettmeier, and Hans-Günther Döbereiner — Institut für Biophysik, Universität Bremen

The slime mold *Physarum polycephalum* is a multi-nucleated but unicellular organism, which amazingly can grow up to square meters. It forms extended vein networks in order to search for food. The structure and dynamics of the foraging units is dependent on environmental conditions and life stage. We find oscillating microplasmodia which percolate into a network directly, see PRL 109, 078103 (2012), or fuse into compact satellites before transforming into networks as well. Here, we present our recent experimental and theoretical results on the formation of satellites. Satellites are found to be predominant after prolonged starvation of microplasmodia. The number of satellites forming out of a spherical patch of single microplasmodia shows characteristic scaling behavior with coverage. Further, we have obtained ultra-structural insights into the morphology and topology of internal and external transport veins.

BP 19.4 Tue 10:30 H 1058

Microcolony Merging of Neisseria Gonorrhoeae is driven by Pili-mediated Cell-Cell Interactions — •Wolfram Pönisch[1], Christoph Weber[1], Khaled Alzurqa[2], Hadi Nasrollahi[2], Nicolas Biais[2], and Vasily Zaburdaev[1] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Brooklyn College, NY, USA

The bacterium Neisseria gonorrhoeae is the causative agent of the second most common sexually transmitted disease gonorrhea. During the infection process bacteria form microcolonies consisting of a few hundreds to a few thousands of individual cells. The attractive cell-cell interactions required for colony formation are mediated by type IV pili, thin and long filaments emerging from the cell membrane. Recently it has been shown how multiple retractile pili coordinate their forces to propel the cells on a surface. While there is evidence that a closely related process causes the cell-cell-interactions, the physical principles driving the formation of the colonies are poorly understood. We examine a key mechanism of colony assembly, the coalescence of two microcolonies, by performing experiments and developing a theoretical microscopic model of individual cells interacting solely by their pili. The comparison of the experimental data and results of our model exhibits an excellent quantitative agreement. Initially two colonies show a fast approach within a few minutes that is followed by a relaxation of the colony shape towards a sphere with a characteristic time of hours. Our findings suggest that pili-mediated interactions are the major mechanism required to explain the merging of microcolonies.

BP 19.5 Tue 10:45 H 1058

Towards the understanding of three-dimensional tissue organization — •Sebastian Ehrig[1], Cécile M. Bidan[2], Philip Kollmannsberger[3], Peter Fratzl[1], and John W. C. Dunlop[1] — [1]Max Planck Institute of Colloids and Interfaces, Germany — [2]Université Joseph Fourier, Grenoble, France — [3]Laboratory of Applied Mechanobiology, ETH Zürich, Switzerland

Biological materials possess an impressive range of mechanical properties due to their intrinsic tissue architecture. However, how these tissues organize to from complex three-dimensional structures over multi-cellular length scales is yet to be resolved. Using new theoretical approaches to self-organization along with 3D tissue culture experiments, we try to understand the dynamics of tissue-organization in 3D.

We recently demonstrated that tissue formation in straight sided pores of controlled shape can be described by a 2D model of curvature controlled growth as verified by subsequent experiments. Further advances in theoretical modeling enabled us to describe the spatial distribution of tissue growth in 3D.

We now develop active particle simulations on curved surfaces to explore the impact of 3D curvature on cell organization that give rise to the formation of complex tissue patterns. Insights into the design principles of the tissue and the role of the geometry of the surrounding environment on growth may have important consequences towards the understanding of tissue remodelling and scaffold design in tissue engineering.

15 min break

BP 19.6 Tue 11:15 H 1058

Epithelial tissue growth and organization: mystery or physics? — •Sara Kaliman[1], Carina Wollnik[2], Damir Vurnek[1], Florian Rehfeldt[2], and Ana-Sunčana Smith[1] — [1]Institut fur Theoretische Physik, FAU, Erlangen — [2]3rd Institute of Physics-Biophysics, Uni Gottingen

Tissue growth is a complex and indisputably important process but despite all the effort in past decades mechanism remains unclear. As model system for such study we have chosen MDCK II cell line seeded on polyacrylamide gels or glass substrates. In most common scenario cluster of cells forms radial monolayers with very dense bulk surrounded by a low density ring of a moving and proliferating edge. To elucidate the mechanism behind compartmentalization to bulk and edge we have simulated cluster growth with Voronoi tessellation model. In the simulation we use measured area growth of the cluster, proliferation rates and speed distribution inside the cluster. Our aim is to distinguish passive from active mechanism during epithelial tissue development. Furthermore, we answer is organization of cells in the tissue random. To do so we compare various morphological parameters of

real tissue with randomly distributed mono-disperse and poly-disperse circles and ellipses. We find that elongation and size distribution of nuclei predetermines cell shapes and correlations in the tissue. Lastly, we write free energy functional as a sum of morphological and elastic term and prove that tissue minimizes energy as it approaches steady state density and undergoes phase transition at intermediate densities when surface tension of cell membrane starts to play a role.

BP 19.7 Tue 11:30 H 1058

Hydrodynamic theory of developing epithelia — •Marko Popovic[1], Raphael Etournay[2], Matthias Merkel[1], Amitabha Nandi[1], Frank Jülicher[1], Suzanne Eaton[2], and Guillaume Salbreux[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 which can deform and flow during animal development. During epithelial deformations, cells can change shape, but can also rearrange their neighbors, divide or be extruded from the tissue. Neighbor rearrangements occur through topological transitions where cell-cell junctions disappear and reform. Topological transitions are an important component of many developmental events. They enable relaxation of shear stress, effectively allowing viscous flows in the epithelium.

We study the pupal wing morphogenesis in the fruit fly D. melanogaster and quantify the contribution of topological transitions to the overall wing shape. The non-trivial pattern of this contribution suggests the existence of active processes driving topological transitions. To understand the mechanics of the developing epithelium, we propose a hydrodynamic theory including the effects of active cellular processes. The theory describes effects of topological transitions and cell shape changes on the tissue shear, thus connecting cellular and tissue scales. Although motivated by the fruit fly wing morphogenesis, our theory is generic and can be applied to other tissues.

BP 19.8 Tue 11:45 H 1058

Dynamics and precision of mouse neural tube patterning — •Marcin Zagórski[1], Anna Kicheva[2], Gašper Tkačik[1], James Briscoe[2], and Tobias Bollenbach[1] — [1]Institute of Science and Technology (IST) Austria, Klosterneuburg — [2]Medical Research Council (MRC), National Institute for Medical Research, London, UK

Early in vertebrate development, different neuronal subtypes are generated from neural progenitor cells arrayed along the dorsal-ventral axis of the neural tube. This pattern of neural progenitors is established by morphogens - signaling molecules secreted by cells in restricted source regions at the tissue boundaries. In the neural tube, the morphogens Shh and BMP form opposing concentration profiles which provide positional information to cells and induce the expression of target genes, such as Nkx6.1 and Pax3, at defined positions. It is not understood how the two morphogen signals and the regulatory interactions between target genes together determine the target gene pattern. To address this issue, we measured the two signaling gradients. We quantified the positional information available to the cells with both direct and Gaussian approximation techniques. Early in development, positional information is high, enabling patterning at a precision of three cell diameters; after 20h, however, precision declines significantly in the middle region. Still, after 30h, the expression boundary between Pax3 and Nkx6.1 is precisely specified in the middle. These results suggest that cells in the central neural tube integrate positional information from two opposing morphogen gradients early in development to achieve precise target gene boundary positions at later stages.

BP 19.9 Tue 12:00 H 1058

Robust balance of stochastic stem cell fate through revesible differentiation — •Philip Greulich[1] and Benjamin D. Simons[1,2] — [1]TCM Group, Cavendish Laboratory, University of Cambridge, Cambridge, UK — [2]Gurdon Institute, University of Cambridge, Cambridge, UK

Adult stem cells are the key players in maintaining healthy tissue. In order to keep the population of cells in a tissue stable, the number of stem cells must stay constant over time, i.e. proliferation and differentiation of stem cells must be perfectly balanced (homeostasis). Otherwise, tissues degenerate or dysplastic lesions develop, which can evolve into cancer. In recent years studies have shown that in many mammalian tissues the stem cell fate (stem cell duplication vs. differentiation) is decided stochastically, with equal chances for gain (duplication) and loss of stem cells (differentiation). Nonetheless, the mechanism to maintain the balance in cell fate outcomes remains largely unknown.

Here I present a non-equilibrium stochastic model for cell fate dynamics, where balance of cell fate outcomes follows automatically from two properties of the cells: (i) the cells' potential to reversibly differentiate independent from cell divisions, (ii) their ability to sense and respond to mechanical cues. The model is able to accurately reproduce experimental cell lineage data of living tissues and, remarkably, shows a high robustness towards failure of regulatory pathways. This mechanism may explain how the stability of the cell population in tissues is maintained, and how robust protection against tumours, despite of high frequency of disrupting mutations, is achieved in living organisms.

BP 19.10 Tue 12:15 H 1058

Optical Modulation Transfer by the Vertebrate Retina — •Kaushikaram Subramanian[1], Zuzanna Blaszczak[2], Matthäus Mittasch[1], Alfonso Garcia Ulloa[1], Jochen Guck[3], and Moritz Kreysing[1] — [1]The Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany — [2]Cavendish Laboratory, University of Cambridge, Cambridge, UK — [3]Biotechnology Center, Technische Universität Dresden, Dresden, Germany

It has puzzled biologists for centuries that the vertebrate retina is inverted with respect to its optical function: photons need to traverse multiple layers of living neuronal tissue before detection by photoreceptor cells. Recent findings indicate that cells situated in this light path might circumvent this unfortunate situation by acting as light guides or minimizing light scattering by adapting their nuclear architecture. Using the concept of modulation transfer functions we yield the retina's transmission properties with respect to spatial frequencies. Results from a study in mice are discussed in the light of i) retinal architecture in terms of lateral cell positioning, ii) shape and orientation of individual cells, and iii) optical contribution of subcellular architecture and size distribution of organelles. We further discuss options to employ this platform to determine the relative significance of distinct layers in imparting transparency to retina by genetic deletion of certain cell types. Taking cue from cellular level studies and theoretical models, the research further aims to incorporate ultrastructure of the retina as the basis of light scattering in sub-wavelength regime to understand and explain its superior optical qualities.

BP 19.11 Tue 12:30 H 1058

Experiments and Model: Buckling instability of Regenerating Tissues — •Benjamin Friedrich[3], Hans Kubitschke[2], and Claus Fütterer[1] — [1]Translational Centre of Regenerative Medicine, Leipzig and Biophysical Tools GmbH, Leipzig, Germany — [2]Experimentalphysik I, Universität leipzig, Leipzig, Germany — [3]Max-Planck Institut für die Physik komplexer Systeme, Dresden, Germany

We propose tissue toroids as an ideal minimal model geometry to quantitatively study regeneration, morphogenesis and wound healing. It minimizes nutrient depletion effects which can even lead to necrosis. We report experiments with *Hydra vulgaris* epithelium revealing that tissue rings fold by an original mechanism. This is accompanied by a highly self-organized acto-myosin string spanning along the inner side of the toroid. This folding initiates a transition to a spherical shape and the full regeneration of viable organism. We propose a minimal theoretical description that conceptualizes this mechanical transition in terms of a buckling instability of the tissue torus driven by active mechanical forces. We predict a critical contractility threshold, in agreement with our experimental observations. This versatile model system allows to study and understand morphological transitions in a well defined minimal set-up.