BP 8: Developmental Processes

Time: Tuesday 9:30–13:00 Location: HÜL 186

Invited Talk BP 8.1 Tue 9:30 HÜL 186

Robustness and Scaling in Embryonic Development — •Naama Barkai — Department of Physics of Complex Systems, Weizmann Institute of Science, Rehovot 76100, Israel — Department of Molecular Genetics, Weizmann Institute of Science, Rehovot 76100, Israel

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Invited Talk BP 8.2 Tue 10:00 HÜL 186

The R8 race: Specifying photoreceptor cells in the developing fly eye — •David Lubensky — University of Michigan, Ann Arbor, MI, USA

Regular patterns of cell fate appear widely in biology. Such patterns also emerge spontaneously, via a Turing instability, in models of diffusible activators and inhibitors, but it remains unclear to what extent biology takes advantage of this fact. I will discuss a quantitative analysis of Drosophila eye development, focusing on the activator-inhibitor system responsible for spacing the R8 photoreceptors that define the eye's regular ommatidial pattern. The R8 lattice grows by turning on the expression of proneural genes at a moving front to create new columns of R8 cells. I propose a model where R8 fate specification occurs when a bistable genetic switch is flipped in a given cell; a template of inhibitory signals from the existing R8 lattice determines where the switch will be flipped in the new column. A consequence of our model is that transient perturbations of one column can change the pattern in all subsequent columns. Most strikingly, the normal triangular lattice can give way to stripes of R8 cells. These predictions are confirmed experimentally by manipulation of the *Notch* and *scabrous* genes. In our model, the relative timing and strength of signals from the template, rather than competition among neighboring cells, determines the eventual R8. If time allows, I will discuss implications of this picture for other related examples of neural fate specification.

BP 8.3 Tue 10:30 HÜL 186

Quantification of leaf vein patterning — •Karen Alim and Erwin Frey — Arnold Sommerfeld Center for Theoretical Physics and CeNS, Department of Physics, Ludwig-Maximilians-Universtät München, Theresienstr. 37, 80333 Munich, Germany

Vein networks are essential in transporting nutrition effectively into all cells of an organism. In plant leaves these vein networks are formed by the opposite transport mechanism, the retraction of the plant hormone auxin. The so formed auxin flow pattern is consistent with the vascular network of the mature leaf. Key factors in the non-uniform transport are the competition of auxin carriers within each cell and the coupling between auxin current and carrier location.

We investigate a microscopic model for the directed auxin transport by carrier proteins performing both computer simulations and analytic calculations. These enable us to identify the relevant biological processes which should be considered for leaf vein patterning. Quantitative results help us to suggest observables and experimental scenarios to measure the kinetic rates governing the active transport.

BP 8.4 Tue 10:45 HÜL 186

Investigating the influence of mechanics on epithelial morphogenesis — •Carina M. Edwards[1], Francesco Pampaloni[2], Ernst H. K. Stelzer[2], and Ulrich S. Schwarz[1,3] — [1]Center for Modelling and Simulation in the Biosciences (BIOMS), University of Heidelberg, Im Neuenheimer Feld 267, 69120 Heidelberg, Germany — [2]EMBL Heidelberg, Meyerhofstrasse 1, 69117 Heidelberg, Germany — [3]University of Karlsruhe, Theoretical Biophysics Group, Kaiserstrasse 12, 76131 Karlsruhe, Germany

Mechanical stress and strain are increasingly being recognized as playing a crucial role in determining tissue size and structure. Because experimentally it is very difficult to measure stress and strain for growing tissues, mathematical modelling is required to correlate stress and strain with biological processes like cytoskeletal remodelling. In order to acquire quantitative data, one needs to combine advanced microscopy techniques with image processing. Here we use light-sheet-based fluorescence microscopy applied to the growth of cysts from Madin-Darby canine kidney (MDCK) cells. Using careful image analysis we extract time-resolved data on cyst and lumen size, and on the number of cells. These results are used to rule out or validate growth models, including those that incorporate mechanical effects. We are also able to look at the effect of gel stiffness on cyst growth.

BP 8.5 Tue 11:00 HÜL 186

Optimal precision of noisy gene expression domains — •Thorsten Erdmann[1], Martin Howard[2], and Pieter Rein ten Wolde[1] — [1]FOM Institute Amolf, Amsterdam, The Netherlands — [2]John Innes Centre, Norwich, United Kingdom

During early embryonic development, the body plan of the adult fruit fly is laid out by spatial patterns of gene expression. To form a viable organism different domains need to be reliably separated against the adverse influence of stochastic noise. A prominent example is the domain of the Hunchback protein. The production of Hunchback proteins is activated by a fluctuating morphogen gradient. In addition, the rate of protein production is subject to strong fluctuations. We theoretically study the spatial positioning of the Hunchback domain boundary for fluctuating protein concentrations. We find that the interplay between spatial and temporal averaging leads to an optimal precision for the Hunchback boundary as a function of protein lifetime. Moreover, the Hunchback domain boundary can be determined with better accuracy than the noisy input.

15 min. break

BP 8.6 Tue 11:30 HÜL 186

Slowing down of genetic oscillations in vertebrate segmentation — •Saul Ares[1], Luis G. Morelli[1], Andrew C. Oates[2], and Frank Julicher[1] — [1]Max Planck Institute for the Physics of Complex Systems — [2]Max Planck Institute of Molecular Cell Biology and Genetics

The subdivision of the vertebrate body axis in a segmented pattern is driven by genetic oscillations in the unsegmented tissue called the Presomitic Mesoderm (PSM). These oscillations form waves of gene expression that start at the posterior of the PSM and move anteriorly to finally stop at an arrest front. In situ snapshots of the PSM display a gene expression pattern of several stripes which are thiner at the anterior. Recently, Gomez et al. [Nature, **454**, 335-339 (2008)] have analyzed experimentally embryos of snake, mouse, chick and zebrafish, measuring the sizes of their PSM and the different number of stripes of cyclic gene expression in each species (from 1 in mouse or chick to up to 9 in snake).

In this contribution we present a Delayed Coupling Theory of vertebrate segmentation that treats the cellular oscillators as phase oscillators coupled with a time delay. Using this theory we analyze the data from Gomez et al. and show for the first time that the way in which oscillators slow down across the PSM is different and characteristic of each species. Together with the PSM size and the collective period of the oscillations, the way in which the oscillator slow down establishes the gene expression pattern setting the number and size of the stripes of cyclic gene expression in the PSM.

BP 8.7 Tue 11:45 HÜL 186

Exploring Fgf8 morphogen gradient in vivo — •Markus Burkhardt, Shuizi Rachel Yu, Matthias Nowak, Jonas Ries, Zdeněk Petrášek, Petra Schwille, and Michael Brand — BIOTEC/ TU Dresden, Tatzberg 47-51, 01307 Dresden, Germany

It is widely accepted that tissue differentiation and morphogenesis in multicellular organisms is regulated by tightly controlled concentration gradients of morphogens. How exactly these gradients are formed and maintained, however, is highly controversial. Here, we present a study in living Zebrafish embryos where we directly examine Fgf8 morphogen mobility and concentration by Fluorescence Correlation Spectroscopy (FCS). Our results support a simple mechanism to form an Fgf8 morphogen gradient in Zebrafish embryos. The study shows the potential of FCS as a quantitative method to investigate morphogen gradients at the single molecule level in developing multicellular organisms.

BP 8.8 Tue 12:00 HÜL 186

Early Keratinocyte Differentiation and Epithelial-Tissue Morphogenesis on Micropillar Interfaces — •Simon Schulz[1], Thorsten Steinberg[2], Eva Muessig[2], Jens Ulmer[1], Niels Grabe[3], Gerda Komposch[2], Pascal Tomakidi[2], and Joachim P. Spatz[1] —

[1]Biophysical Chemistry, University of Heidelberg, and Max-Planck-Institute for Metals Research, Stuttgart, Germany. — [2]Department of Orthodontics and Dentofacial Orthopedics, Dental School, University of Heidelberg — [3]Department of Medical Informatics, University of Heidelberg

Proliferation and differentiation of keratinocytes play a crucial role in tissue epithelial tissue integrity. Furthermore connective-tissue fibroblasts are pivotal for epithelial-tissue morphogenesis. The combination of material technologies mimicking different tissues with life sciences can lead to the elucidation of fundamental requirements needed for the cells to properly exert tissue specific functions. We fabricated fibronectin covered polydimethylsiloxane (PDMS) micropillar arrays which can be varied in pillar stiffness, diameter and distance. They are applied as a biomechanical microenvironment for immortalized human gingival keratinocytes (IHGKs) and gingival connective-tissue fibroblasts (GCTFs). Qualitative and quantitative differences in expression of the early keratinocyte differentiation markers keratin 1 and 10 could be observed by varying the pillar distances. We show that co-cultures of GCTFs and IHGKs could also be established. Epithelial equivalents of the IHGKs were grown on these topologically defined environments.

BP 8.9 Tue 12:15 HÜL 186

Determinants of Epithelial Morphogenesis Studied in 3D with Light Sheet-Based Fluorescence Microscopy — •Francesco Pampaloni[1], Carina M. Edwards[2], Ulrich S. Schwarz[2,3], and Ernst H.K. Stelzer[1] — [1]EMBL Heidelberg, Meyerhofstr. 1, D-69117 Heidelberg, Germany — [2]Center for Modelling and Simulation in the Biosciences (BIOMS), University of Heidelberg, Im Neuenheimer Feld 267, 69120 Heidelberg, Germany — [3]University of Karlsruhe, Theoretical Biophysics Group, Kaiserstrasse 12, 76131 Karlsruhe, Germany

Understanding how mechanical forces regulate tissue growth is a major issue in biophysics. Since D'Arcy Thompson published his classical work "On Growth and Form" in 1917, it has been recognized that physical interactions with the environment are as essential as chemical cues for an organism's growth, shape, and function. However, these physical aspects can only be understood in a systematic and quantitative approach where biological data is recorded with high reproducibility, high statistics, and minimum perturbation of the sample. New microscopy techniques, such as light-sheet-based fluorescence microscopy (e.g. SPIM) enable to do that by minimizing photodamage and collecting light with high quantum efficiency. We have employed SPIM to study the growth of multicellular MDCK cysts in 3D collagen gel and matrigel (a widespread model of kidney development). We recorded the growth of 50 MDCK cysts with live fluorescence microscopy measuring the increase of volume and the number of cells and have studied how cyst growth depends on the collagen density.

BP 8.10 Tue 12:30 HÜL 186

Morphogen dynamics and growth control during development — •Peer Mumcu[1], Thomas Bittig[1], Ortrud Wartlick[2], Anna Kicheva[2], Marcos González-Gaitán[2], and Frank Jülicher[1] — [1]Max Planck Institute for the Physics of Complex Systems, Nöthnitzer Straße 38, 01187 Dresden — [2]Department of Biochemistry and Department of Molecular Biology, Geneva University, Sciences II, Quai Ernest-Ansermet 30, 1211 Geneva 4, Switzerland

Growing organs in developing animals have the ability to control their size and shape autonomously. Morphogens are a special class of signaling molecules which play a key role in this process. They are secreted from localized sources and spread throughout the growing tissue where they are degraded. They thereby form graded concentration profiles which provide the target tissue with positional information. We present a theoretical study of the transport of morphogens in growing epithelia using a continuum theory and a two-dimensional vertex model. In the vertex model the adherence junctions of the cells are represented as a network of polygons and morphogen transport is described by a diffusion current between neighbouring cells. Within this framework we study the dynamics of the morphogen gradient and we discuss the relationship between the spatio-temporal morphogen levels and the growth rate of the tissue during development. We compare our theory to experimental data from the developing Drosophila wing imaginal disc, a precursor of the fly wing.

BP 8.11 Tue 12:45 HÜL 186

Dynamics of Polar and Hexagonal Order in Developing Epithelia — •Reza Farhadifar[1], Benoit Aigouy[2], Douglas B. Staple[1], Jens Roeper[2], Andreas Sanger[2], Suzanne Eaton[2], and Frank Jülicher[1] — [1]MPI-PKS, Dresden, Germany — [2]MPI-CBG, Dresden, Germany

Planar cell polarity (PCP) is a tissue-level phenomenon that coordinates cell behavior in epithelia, which are two-dimensional tissues. A particular example of planar cell polarity at work is revealed in the orientation pattern of hairs, which form on the wing of the fruit fly Drosophila. Planar polarity is established by a molecular organization that includes an asymmetric distribution of PCP proteins within cells. The distribution of these proteins in a given cell determines of the polarity of neighboring cells. At the end of wing development, a specific pattern of PCP orientational order is established. We present a theoretical study of planar polarity in developing epithelia based on a vertex model, which can account for cell shape and cell mechanics. The distribution of PCP molecules along cell boundaries as well as their interactions with neighboring cells are captured in a coarse grained description. We identify a basic mechanism by which long-range correlations throughout the tissue can be established. We furthermore study the role of quasi-static shear deformations. In the presence of shear, the polarity of the tissue reorients. In addition, hexagonal order emerges under these conditions. These physical mechanisms for ordering can account for the processes observed during development of the Drosophila wing.