BP 36: Posters: Tissue Dynamics, Charge Effects, and Anomalous Transport

Time: Thursday 17:15–20:00 Location: Poster B2

BP 36.1 Thu 17:15 Poster B2

Self-organized growth regulation in developing epithelia — •Peer Mumcu[1], Thomas Bittig[1], Ortrud Wartlick[2], Marcos González-Gaitán[2], and Frank Jülicher[1] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Department of Biochemistry and Department of Molecular Biology, Geneva University, Switzerland

Developing tissues possess intrinsic growth control mechanisms which determine the final size and shape. The basic principles of growth regulation are still poorly understood but it is widely accepted that certain morphogens act as growth factors that play a key role in this process. Morphogens are a special class of signaling molecules which are secreted from localized sources, spread throughout the tissue and provide cells with positional information. Focusing on the Drosophila fly wing as model system, we present a theoretical study of dynamical morphogen distributions in growing epithelia using a continuum theory and a description which is based on discrete cells. The discrete description combines a two-dimensional vertex model for the organization of cells with dynamic equations for the morphogen concentrations. Within this framework we discuss the scaling of morphogen profiles with tissue size. We introduce a growth rule which couples the decision to divide a cell with temporal changes of the cellular morphogen levels. We show that this growth rule can regulate growth in a self-organized way and compare the results to experimental data from the developing fly wing.

BP 36.2 Thu 17:15 Poster B2

An Asymmetric her Gene Regulatory Network in the Segmentation Clock — •Saúl Ares[1], Christian Schröter[2], Luis G. Morelli[1,2], Andrew C. Oates[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

The segmentation clock is a transcriptional oscillator that controls the sequential segmentation of the vertebrate body axis during embryonic development. Previous models of the zebrafish segmentation clock consisting of symmetric interactions of the cyclic genes *her1* and *her7* were based only on wild type gene expression data. We have combined genetic experiments studying mutations in both these genes and in the non-cyclic *hes6*, together with measurements of the period of oscillation of the several mutant conditions. Our results can not be explained by previous models. To understand them, we propose a new model where the *her* genes have distinct functions in the segmentation clock with asymmetric interactions between them. Our mathematical model is based on a genetic regulatory network where *her1/hes6* and *her7/hes6* heterodimers have opposing functions. This genetic network model is consistent with experiments and makes testable predictions of biochemical interactions in the clockwork. An important insight coming from our model is that heterodimer formation is a rate limiting step and hence plays a key role in control of the segmentation period.

BP 36.3 Thu 17:15 Poster B2

Intercellular coupling tunes the period and stability of a multicellular biological clock — •Luis G. Morelli[1,2], Saúl Ares[2], Leah Herrgen[1], Christian Schröter[1], Andrew C. Oates[1], and Frank Jülicher[2] — [1]Max Planck Institute of Molecular Cell Biology and Genetics — [2]Max Planck Institute for the Physics of Complex Systems

During vertebrate embryonic development, the body segments are formed in a sequential and periodic process controlled by a multicellular genetic clock. Single cells contain autonomous genetic oscillators, and communicate with their neighbors to produce a reliable rhythm that results in a precise segmented pattern. Intercellular communication involves a complex cascade of events that introduces time delays in the coupling, and coupling delays can have complex effects on the collective dynamics. We have developed a generic description of the segmentation clock using phase oscillators, coupled with a time delay. This theory predicted that coupling strength and delays can tune the period of the segmentation clock and produce changes in segment length and cyclic gene expression patterns. We have verified these predictions under experimental conditions affecting components of intercellular coupling in zebrafish embryos. The theory also predicts the existence of instabilities for certain ranges of the coupling delay. By altering the traffic of ligands involved in inter-cellular communication, we find evidence consistent with such an instability.

BP 36.4 Thu 17:15 Poster B2

Vertex Model for Mechanics and Dynamics of Epithelia — •Douglas B. Staple[1], Reza Farhadifar[1], 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 sheets of cells that organize into specific geometrical arrangements or morphologies essential for proper tissue functioning. Here we represent epithelia as networks of polygons: stable and stationary network configurations obey force balance and are represented as local minima of a work function. We describe the ground-state phase diagram to our model, identifying transitions relevant to tissue growth, mechanics, and cell extrusion. The dynamics of cell extrusion and cell-boundary rearrangements depend critically on energetic barriers arising naturally in our model, and are well understood in terms of simple geometric arguments.

BP 36.5 Thu 17:15 Poster B2

Simulation and analysis of neuronal pattern formation in the visual cortex — •Ghazaleh Afshar[1,2], Dominik Heide[5], Lars Reichl[1,2], and Fred Wolf[1,2,3,4] — [1]MPIDS, Göttingen — [2]BCCN, Göttingen — [3]Georg-August-Universität, Göttingen — [4]IMPRS, Göttingen — [5]FIAS, Frankfurt am Main

Orientation preference maps in the visual cortex, characterized by topological point defects called pinwheels, presumably develop by self-organization of neuronal circuits [1,2]. It was shown recently that the spacing of adjacent orientation columns exhibits a high degree of variability within the visual cortex [3]. We generalized a model based on Turing type instability proposed previously [1] to exhibit a map of local column spacing instead of a single fixed wavelength and studied this model numerically. In the homogeneous model defect densities of solutions split at a late stage of development filling a broad band of values. In the model with spacing heterogeneity this splitting is suppressed. In contrast to the homogeneous model in which the power spectrum of the stable solutions is composed of a finite number of Fourier components, in the heterogeneous model the power spectrum asymptotically shows a continuous band of modes around the critical circle with a finite width depending on the strength of spacing inhomogeneity. This closely resembles the experimental observation. We conclude that wavelength heterogeneity substantially increases the agreement between experimental observation and Turing type models of neural pattern formation. [1] Wolf. PRL (2005). [2] Kaschube et al. NJP (2008). [3] Kaschube et al. PNAS (2009).

BP 36.6 Thu 17:15 Poster B2

Solid tumor growth and fluid transport taking into account a hierarchical network of the host: a three-dimensional theoretical model — •Michael Welter and Heiko Rieger — Universität des Saarlandes, 66041 Saarbrücken, Germany

Solid tumors like melanoma acquire sufficient nutrients by coopting the host vasculature and inducing angiogenesis in the surrounding tissue. Furthermore their growth is accompanied with a drastic reduction of vessels density and vessel dilation in the center of the tumor. Thus the original well organized hierarchical network becomes chaotic and a heterogeneously distributed tumor vasculature is formed. We develop a hybrid stochastic/continuum model for three-dimensional tumor growth which includes an explicit representation of the hosts vasculature and its remodeling via sprouting, vessel removal and dilation. The evolution of the tumor mass is captured by a diffusion-reaction model. The heterogeneity and leakiness of tumor vessels is highly relevant for the exavasation and interstitial transport of drugs since large non-vascularized regions exist and high interstitial fluid pressures may impede flow through the vessel walls. Therefore we analyze the flow of a tracer through the interstitial space coupled to our tumor networks by means of a convection-diffusion-reaction model.

BP 36.7 Thu 17:15 Poster B2

Ion Transport through OmpF and OmpC Channels Simulated

using Molecular Dynamics — Soroosh Pezeshki, Istvan Biro, Mathias Winterhalter, and •Ulrich Kleinekathöfer — Jacobs University Bremen, Campus Ring 1, 28759 Bremen, Germany

The outer membrane porins F and C (OmpF and OmpC) are major pores in the cell membrane of the Gram-negative bacterium *Escherichia coli*. They are considered the main pathways for ions and molecules through the membrane. Using the crystal structures, it is possible to study OmpF and OmpC in computer simulations. The ion conductance through these nano pores is simulated in all-atom molecular dynamics and the temperature dependence of the conductance is calculated for different salt concentrations. Good agreement can be observed in the comparison between simulations and experiments [1]. The advantage of molecular dynamics simulations is that they allow a deeper view on the molecular interactions leading to the macroscopic observation. Ion pathways can be followed and the interaction of ions with certain residues can be observed [2].

[1] S. Pezeshki, C. Chimerel, A. Bessenov, M. Winterhalter, U. Kleinekathöfer, Biophys. J. **97**, 1898 (2009).

[2] C. Chimerel, L. Movileanu, S. Pezeshki, M. Winterhalter, U. Kleinekathöfer, Eur. Biophys. J. **38**, 121 (2008).

BP 36.8 Thu 17:15 Poster B2

Charge induced liquid-liquid phase separation in protein solutions — •Marcell Wolf, Zhang Fajun, and Schreiber Frank — Institut für Angewandte Physik, Universität Tübingen, Auf der Morgenstelle 10, 72076 Tübingen, Germany

The liquid-liquid phase separation (LLPS) in concentrated protein solutions plays an important role for protein crystallisation as well as protein-association related diseases, such as the sickle cell anemia and eye cataracts, etc. Here, we show that the LLPS in protein solutions can be induced by using a multivalent salt, using Human Serum Albumin (HSA) and Yttrium Chloride (YCl3). The phase diagram of HSA with YCl3 was determined; it shows a re-entrant phase behaviour [1], i.e. the protein solution undergoes a phase-separation upon adding salt up to a critical value c*, c**, causes the precipitate to dissolve an the system turns back to a homogeneous solution. In the condensed phase between c* and c** the solution exhibits a (L-L) phase separation. After centrifugation, a protein-poor and a protein-rich phase were obtained and the protein concentration for each phase was determined using UV-visible spectroscopy. We also discuss the effect of the LLPS conditions for protein crystallisation.

[1] F. Zhang et al., Phys. Rev. Lett. 101 (2008) 148101

BP 36.9 Thu 17:15 Poster B2

Reentrant Condensation of protein solutions induced by Fe^{3+} and Al^{3+} — •Benjamin Heck, Fajun Zhang, and Frank Schreiber — Auf der Morgenstelle 10, Universitaet Tuebingen,72076 Tuebingen, Germany

The trivalent ions such as Fe^{3+} can be physiologically important and also relevant in the context of protein-aggregation diseases such as Alzheimer. Therefore it is important to understand their impact on protein interactions and phase behavior in solution. Using model globular proteins, we found that addition of Fe^{3+}/Al^{3+} into protein solution leads to a reentrant phase behavior [1]. When salt concentration, c, is below a critical value, c<c*, proteins are negatively charged. The repulsive Coulomb interaction is dominating which stabilizes proteins in solution. Above c*, aggregation occurs because the effective surface charge of proteins is significantly reduced due to the binding of cations on the protein surface. Further increase salt concentration above a second critical value, c**, one finds redissolution which in a simple picture is interpreted as effective inversion of charges [1].Charge inversion takes place only for multivalent ions. Electrophoresis experiments confirm the effective charge inversion of proteins as a function of salt concentration. Small-angle X-ray scattering data further reveal a clear transition of interactions from repulsive to attractive and to repulsive again at c<c*, c*<c<c** and c**<c, respectively. [1] F. Zhang et al., Phys. Rev. Lett. 101 (2008) 148101

BP 36.10 Thu 17:15 Poster B2

Anomalous transport in living cells — •Doris Heinrich — Biophysics of Cell Dynamics Group, Fakultät für Physik und CeNS, LMU München, Germany

Living cells exhibit exceptional dynamic properties, caused by the presence of ATP-driven motion. In particular, intracellular transport of cargos proceeds by successive phases of diffusion and active movement along microtubules via dynein and kinesin motors. While passive Brownian motion allows for intracellular transport of molecules on the nanoscale, it becomes inefficient for transport of large proteins, vesicles and organelles on the scale of a whole cell. We developed an automated and reliable time-resolved identification method for motility state signatures of cytoplasmic tracers. Such an approach is both experimentally challenging and of fundamental importance for our understanding of intracellular transport processes. We investigated the motion of micron- and nanosized particles in the amoeba Dictyostelium discoideum (Dd). The distribution of active transport durations is found to decay exponentially with a characteristic time t = 0.65 s. The velocity distribution of active events exhibits several peaks, revealing the signature of a finite number of molecular motors working collectively. By further applying spatially and temporally defined external boundary conditions to these cells, like drugs, precisely monitored magnetic field gradients or by cell motility essays on pre-ordered 3D topologies, we induce changes in cellular function.

BP 36.11 Thu 17:15 Poster B2

Non-ballistic and subdiffusive nanoparticle transport in living cells — •Marcus Otten[1], Amitabha Nandi[2], Delphine Arcizet[1], Benjamin Lindner[2], and Doris Heinrich[1] — [1]Ludwig-Maximilians-Universität and Center for NanoScience (CeNS), München, Germany — [2]Max-Planck-Institut für Physik komplexer Systeme, Dresden, Germany

Intracellular transport of vesicles, macromolecules and organelles relies on ballistic and diffusive (including subdiffusive, Brownian and superdiffusive) motion. Local mean square displacement (MSD) analysis allows for the time-resolved separation of these two motion types and their respective motion parameters. It has been established that the ballistic regime is determined by molecular motors. The diffusive regime is of particular interest for inferring information about the cytoskeleton's role in transport.

The non-ballistic phases of intracellular transport are characterized experimentally using nanoparticles in Dictyostelium discoideum cells. Local MSD analysis yields the distributions for the effective diffusion coefficient and the local MSD exponent. These statistics can be reproduced by simulating a Brownian motion the increments of which are negatively correlated over short times. Very good agreement of the experimental and simulated statistics yields valuable information about the short-timescale subdiffusive behaviour and an underlying biophysical picture.