BP 22: Transport Processes and Cellular Trafficking

Time: Thursday 14:30–17:00 Location: ZEU 260

BP 22.1 Thu 14:30 ZEU 260

Modelling anisotropy in protein encounter: a Langevin equation approach with reaction patches — •Jakob Schluttig and Ulrich S. Schwarz — University of Karlsruhe, Theoretical Biophysics Group, Kaiserstrasse 12, 76131 Karlsruhe, Germany

Protein association involves anisotropy for at least two reasons. First the shape of proteins might be non-spherical and thus their diffusion matrix is not necessarily diagonal. Second the association process itself is anisotropic because the binding interfaces are localized at specific positions on their surface. We implemented a Langevin equation approach with reaction patches which allows us to study these two effects [1]. For spherical proteins we find that encounter frequency scales linearly with protein concentration, thus proving that our microscopic model results in a well-defined macroscopic encounter rate. For specific systems of interest and appropriate choices for the size of the reaction patches, encounter rates are obtained within one order of magnitude of the experimentally measured association rates. The number of unsuccessful contacts before encounter decreases with increasing encounter rate and ranges from 20-9000. For spheroids, the principal diffusion coefficients are known analytically and do only sublinearly depend on the ratio ξ of the spatial dimensions. Furthermore the crossover from anisotropic to isotropic diffusion caused by rotational diffusion can be evaluated analytically. These analytical results suggest that the effect of varying ξ on the encounter rate is rather weak, as indeed confirmed by computer simulations.

[1] J. Schluttig et al., J. Chem. Phys. **129**, 155106 (2008).

BP 22.2 Thu 14:45 ZEU 260

Time-resolved analysis of active and passive transport in living cells — •Doris Heinrich[1], Delphine Arcizet[1], Börn Meier[1], Erich Sackmann[2], and Joachim Rädler[1] — [1]Biophysics of Cell Dynamics Group at the Chair of Soft Condensed Matter and Biophysics, Fakultät für Physik und Center for NanoScience (CeNS), Ludwig-Maximilians Universitaet, D-80539 Muenchen, Germany — [2]Physik Department E22, Technische Universitaet Muenchen, D-85748 Garching, Germany

The cellular cytoskeleton is a fascinating active network with exceptional dynamic properties due to the presence of ATP-driven motion. In particular, intracellular transport of cargos is effectively mediated by successive phases of diffusion and active cargo movement along microtubule filaments. We investigated the active and passive intracellular transport phenomena by tracking tracer particles in Dictyostelium discoideum cells and analysing the traces with a novel time-resolved mean-square displacement algorithm [1]. By reliably separating both motion types in a statistical analysis, we were able to determine active velocity distributions as well as diffusion coefficient distributions. The exponential decay of active lifetimes reveals a characteristic life time of cargos on microtubules of t=0.65 s. Further, the active velocity distributions exhibit several peaks, revealing the signature of a finite number of molecular motors working collectively.

[1] D. Arcizet, B. Meier, E. Sackmann, J. Raedler and D. Heinrich. Temporal Analysis of Active and Passive Transport in Living Cells, Phys. Rev. Lett., in press

BP 22.3 Thu 15:00 ZEU 260

Fluorescence correlation analysis of protein dynamics in dividing *C. elegans* embryo — •Zdeněk Petrášek[1], Carsten Hoege[2], Anthony A. Hyman[2], and Petra Schwille[1] — [1]Biophysics group, Biotechnologisches Zentrum, TU Dresden, Germany — [2]Max Planck Institute of Molecular Biology and Genetics, Dresden, Germany

We have combined two-photon fluorescence correlation spectroscopy (FCS), scanning FCS (sFCS) and time-lapse imaging to study the localization and motion of several GFP-labelled proteins involved in the asymmetric first division of *C. elegans* embryo. The diffusion of all investigated proteins in the cytosol, where they are distributed homogeneously on the scale of optical resolution, was measured with a standard FCS, yielding a distribution of diffusion coefficients. The comparison of the protein size and the obtained diffusion coefficients indicates hindered diffusion or formation of larger complexes.

Two of the investigated proteins, known to play an essential role in the first asymmetric division, PAR-2 and NMY-2, are non-uniformly distributed on the embryo cortex. Their motion was characterized by spatio-temporal correlation measured with sFCS. Scanning FCS reduces the effects of dye photobleaching and improves the statistical accuracy, making it possible to study even slow protein dynamics. The PAR-2 cortical pattern is less concentrated into discrete spots and more dynamic than that of NMY-2, indicating predominantly independent localization of the two proteins on the cortex.

BP 22.4 Thu 15:15 ZEU 260

A dynamic model for the morphogenesis of the Golgi apparatus — •Jens Kuehnle[1,2], Julian Shillcock[2], Ole G. Mouritsen[2], and Matthias Weiss[1] — [1]DKFZ, Heidelberg, Germany — [2]Memphys-Center, University of Southern Denmark

While there has been considerable progress in understanding the molecular biology of the secretory pathway of mammalian cells, the fundamental question of how the most prominent and complex organelle of the pathway, the Golgi apparatus, is formed and maintained has remained largely elusive. Using a minimal self-organizing scheme based on incoming transport from the nearby endoplasmic reticulum and aging of Golgi fragments ('cisternal maturation'), we are able to explain the de novo formation of a Golgi apparatus. Moreover, we can determine a region of the models phase space for which secretion rates support the formation of a proper stack of Golgi cisternae. Our simulations are consistent with analytical considerations and agree well with existing experimental data.

BP 22.5 Thu 15:30 ZEU 260

Spot biopolymer motion by NMR — •Michael Kovermann, Martin Schöne, and Jochen Balbach — Institut für Physik/Fachgruppe Biopyhsik, Martin-Luther-Universität Halle-Wittenberg, Betty-Heimann-Straße 7, 06120 Halle/Saale, Germany

The dynamics and the motional behaviour of a protein are important parameters to describe a protein and to understand its function. To learn more about this we characterized the translational motion of various peptides and proteins in solution.

By using a diffusion measurement setup running on an NMR spectrometer we are able to determine the hydrodynamic radius of biopolymers. We compare the correlation times extracted from the diffusion measurements (and known viscosity) with the values from ^{15}N relaxation measurements. From these data we are able to conclude whether the overall tumbling of the biopolymer inside the hydration shell is, on the one hand, caused by the microviscosity or, on the other hand, by the size of the protein.

Additionally we are able to follow a kinetic reaction (fibrillation of the amyloid protein Aβ) which revealed an increase of the hydrodynamic radius by the fibrillation time. This property cannot be observed by using only the signal intensity in the NMR spectrum.

15 min. break

BP 22.6 Thu 16:00 ZEU 260

Elucidating the random process behind crowding-induced subdiffusion — •Marcel Hellmann[1,2], Dieter W. Heermann[2], and Matthias Weiss[1] — [1]German Cancer Research Center, Cellular Biophysics Group (BIOMS), Im Neuenheimer Feld 280, D-69120 Heidelberg — [2]Universität Heidelberg, Institut für Theoretische Physik, Philosophenweg 19, D-69120 Heidelberg

Complex and crowded media are a widespread phenomenon. A prominent example is the cytoplasm of living cells. The presence of filamentous structures and a plethora of embedded macromolecules strongly affect the mobility of tracer particles. Experiments have shown a subdiffusive behavior of tracers with a nonlinear growth of the mean square displacement: $\langle x^2 \rangle \sim t^\alpha$, $\alpha \sim 0.7$ (Weiss *et al.*, Biophys. J.; Guigas *et al.* Biophys J; FEBS Lett.).

Two competing mathematical models have been proposed to rationalize this experimental observation: The continuous time random walk (CTRW) and fractional Brownian motion (fBM). Owing to their distinct propagators (non-Gaussian and Gaussian-like, respectively), these two models make distinct predictions, e.g. concerning the breaking of ergodicity. To explore which of the two models may explain the experimental findings, we have used mesoscopic computer simulations. In particular, we have investigated the diffusion of tracer particles in a crowded environment that mimics the cytoplasm. Our data sug-

gest that crowding-induced subdiffusion relies on (weakly) attractive interactions of the macromolecules.

BP 22.7 Thu 16:15 ZEU 260

Protein diffusion in crowded solutions: A quasi-elastic neutron scattering study — •Felix Roosen-Runge[1,2], Marcus Hennig[1,2], Fajun Zhang[1], Stefan Zorn[1], Maximilian Skoda[3], Robert M.J. Jacobs[4], Tilo Seydel[2], and Frank Schreiber[1] — [1]Institut für Angewandte Physik, Universität Tübingen, Germany — [2]Institut Laue-Langevin, Grenoble, France — [3]ISIS, Didcot, UK — [4]Chemistry Research Laboratory, Oxford, UK

In a typical living cell, proteins function in a relatively crowded cytoplasmic environment where up to 40% of the space is occupied by various biomacromolecules. We present a quasi-elastic neutron scattering (QENS) study of protein dynamics under the condition of "protein crowding" in solution. Using the protein bovine serum albumin (BSA) as model, we studied the protein dynamics as a function of protein concentration, ionic strength and temperature in order to address self-diffusive motions on nanosecond time scales. The dynamics was studied by neutron backscattering scans performed at selected temperatures ranging from 280K up to 325K. The relaxation times and diffusion coefficients extracted from the fits for various states of the BSA solution (temperature, BSA and salt concentration) are analyzed. It was found that salt addition has no significant effect on the relaxation rates on length scales commensurate with protein nearest-neighbor distances, whilst temperature has a strong effect on the diffusive motion of BSA. Charge effects including ionic strength and valence are further addressed by complementary SAXS data.

BP 22.8 Thu 16:30 ZEU 260

Diffusional properties of unfolded proteins — •Nina Malchus and Matthias Weiss — German Cancer Research Center, Heidelberg, Deutschland

The diffusion characteristics of tracer particles in complex systems reveals properties of the surrounding medium and its interaction with the tracer. Using fluorescence correlation spectroscopy (FCS), we have examined the diffusion of folded and unfolded membrane proteins in the endoplasmatic reticulum (ER) of living cells to elucidate the interactions of unfolded proteins with the chaperone machinery. Both, folded and unfolded proteins, show anomalous diffusion with a mean square displacement $\propto t^{\alpha}$, $\alpha < 1$. For unfolded proteins the anomaly was significantly stronger, i.e. α was lower. Disrupting the interaction between chaperones and unfolded proteins resulted in a shift of the anomaly to the values observed for folded proteins. Accompanying computer simulations indicate that obstructed diffusion in the ER and complex formation of chaperones and unfolded proteins are responsible for the observed phenomena. This prediction is well supported by additional experiments.

BP 22.9 Thu 16:45 ZEU 260

Hydrophobic Mismatch: A universal Tool for Clustering, Demixing and Sorting of Transmembrane Proteins — •Ulrich Schmidt, Gernot Guigas, and Matthias Weiss — German Cancer Research Center, Cellular Biophysics Group (BIOMS), Im Neuenheimer Feld 280, D-69120 Heidelberg

Sorting of transmembrane proteins is a central task of eukaryotic cells, in particular in the secretory pathway. Due to a lack of an organizing mastermind, the decision wether a membrane protein participates in secretory transport or not has to be made by a self-organizing process on the molecular scale, e.g. via cluster formation. We show by means of coarse-grained membrane simulations that hydrophobic mismatching can drive cluster formation of transmembrane proteins [1]. Also, proteins with different degrees of hydrophobic mismatching can segregate and form homo-oligomers. In addition, we show that proteins partition into the lipid phase with the smallest hydrophobic mismatch if the membrane has a heterogeneous composition. Our data thus indicate that hydrophobic mismatching may help to organize trafficking along the secretory pathway in living cells.

[1] U. Schmidt, G. Guigas & M. Weiss, Phys. Rev. Lett. 101, 128104 (2008)