BP 1: Proteins I

Time: Monday 9:30–13:00 Location: H 1058

Topical Talk BP 1.1 Mon 9:30 H 1058

Friction and Hydration Repulsion Between Hydrogen-Bonding Surfaces — •Roland Netz — FU Berlin

The dynamics and statics of polar surfaces are governed by the hydrogen-bonding network and the interfacial water layer properties. Insight can be gained from all-atomistic simulations with explicit water that reach the experimentally relevant length and time scales. Two connected lines of work will be discussed: 1) On surfaces, the friction coefficient of bound peptides is very low on hydrophobic substrates, which is traced back to the presence of a depletion layer between substrate and water that forms a lubrication layer. Conversely, friction forces on hydrophilic substrates are large. A general friction law is presented and describes the dynamics of hydrogen-bonded matter in the viscous limit. 2) The so-called hydration repulsion between polar surfaces in water is studied using a novel simulation technique that allows to efficiently determine the interaction pressure at constant water chemical potential. The hydration repulsion is shown to be caused by a mixture of water polarization effects and the desorption of interfacial water.

BP 1.2 Mon 10:00 H 1058

Temperature-induced denaturation of protein layers at solid-liquid interfaces - an x-ray reflectivity study — •Irena Kiesel[1], Michael Paulus[1], Julia Nase[1], Sebastian Tiemeyer[1], Christian Sternemann[1], Anne K. Hüsecken[2], Steffen Bieder[1], and Metin Tolan[1] — [1]Fakultät Physik/DELTA, TU Dortmund, Maria-Goeppert-Mayer-Str. 2, 44227 Dortmund, Germany — [2]Naturwissenschaftlich Technische Fakultät, Fachbereich Physik, Universität Siegen, Walter-Flex-Str. 3, 57068 Siegen, Germany

Protein adsorption at solid-liquid interfaces is crucial for many applications such as in food industry and medical devices. As proteins loose their functionality during denaturation, the state of the adsorbed proteins influence the growth of biofilms (e.g. bacteria) and the acceptance of implants in human body (e.g. growth of cells). Our aim is to understand the denaturation process of proteins at the solid-liquid interface. Until now, most denaturation processes were analysed in protein solutions, which serves as a protein reservoir. We investigate the protein denaturation process in two different environments by heating adsorbed protein layers up to 90° C and analyse them at each temperature step by x-ray reflectivity measurements. Therefor we use the 27 keV x-ray reflectivity set-up at BL9 at the synchrotron light source DELTA, Dortmund. The denaturation process is investigated by analyzing the (layer) electron density profile and with this, information on structural changes in the protein film induced by temperature are obtained.

BP 1.3 Mon 10:15 H 1058

The influence of van der Waals forces on protein adsorption kinetics — •Almuth Hoffmann, Hendrik Hähl, and Karin Jacob — Saarland University, D-66123 Saarbrücken, Germany

In contact with an aqueous solution of proteins, any surface is instantly covered by a thin layer of proteins. It is of great interest for many biological and biomedical applications to understand and control this adsorption process that depends on a multitude of parameters. Concentrating on the influence of the substrate on the adsorption, the surface chemistry has been in focus of many studies. Protein adsorption is mainly influenced by short-range forces arising from the surface chemistry and Coulomb interaction. Yet, it could be shown that proteins also interact with the bulk substrate via van der Waals forces [1,2]. In the present study we show that the adsorption kinetics (as observed by ellipsometry) is affected by the subsurface composition of the substrate. The results are corroborated by simulations, which predict an influence of the van der Waals forces on surface processes (e.g. reorientations, spreading, *) that take place immediately after the initial adsorption. The variation of these surface processes can be investigated by fitting the experimental data with the appropriate model. The rate constants of the surface processes then give insight into the influence of the van der Waals forces.

[1] A. Quinn et al., EPL 81 (2008) 56003.
[2] Y. Schmitt, H. Hähl et al., Biomicrofluidics 4 (2010) 032201.

BP 1.4 Mon 10:30 H 1058

Sequence Independent DNA-to-DNA Binding at a Gold Surface Mediated by a Dimeric Protein — •Tihomir Solomun[1], Alexander Kovalev[1], Robert Wild[2], Harald Seitz[2], and Heinz Sturm[1,3] — [1]Federal Institute for Materials Research and Testing, Unter den Eichen 87, D-12205 Berlin, Germany — [2]Fraunhofer Institut für Biomedizinische Technik, Am Mühlenberg 13, D-14476 Potsdam-Golm, Germany — [3]Technical University Berlin, Pascalstrasse 8-9, D-10587 Berlin, Germany

Confocal fluorescence, surface plasmon resonance (SPR) and atomic force microscopy (AFM) methods were used to study the interaction of a dimeric gene-5-protein (g5p) with an adlayer of single-stranded DNA (ssDNA) oligonucleotides tethered to a gold surface. The data show that a highly stable g5p-ssDNA surface complex is readily formed. The extent of the complexion indicates involvement of cooperative protein-protein interactions. In the case where oligonucleotides are also present in the solution, sequence independent binding takes place between the non-complementary oligonucleotides in the solution and those immobilized on the surface. This binding is rendered possible by dimeric nature of the g5p protein.

BP 1.5 Mon 10:45 H 1058

A novel computer simulation method for simulating the multiscale transduction dynamics of signal proteins — •Emanuel Peter, Bernhard Dick, and Stephan Baeurle — Universität Regensburg, Universitätsstr. 31, 93053 Regensburg

Signal proteins are able to adapt their response to a change in the environment, governing in this way a broad variety of important cellular processes in living systems. While conventional molecular-dynamics (MD) techniques can be used to explore the early signaling pathway of these macromolecules at atomistic resolution [1], their high computational costs limit their usefulness for the elucidation of the multiscale transduction dynamics of most signaling processes, occurring on experimental timescales. To cope with the problem, we introduce in this presentation a novel multiscale-modeling method, based on a combination of the kinetic Monte-Carlo- (KMC) and MD-technique, and demonstrate its suitability for investigating the signaling behavior of the photoswitch light-oxygen-voltage-2-Jα domain from Avena Sativa (AsLOV2-Jα) and an AsLOV2-Jα-regulated photoactivable Rac1-GTPase (PA-Rac1). These applications demonstrate that our approach reliably reproduces the signaling pathways of complex signal proteins, ranging from nanoseconds up to seconds at affordable computational costs [2].

[1] E. Peter, B. Dick, S. A. Baeurle, *Nat.Commun.* (2010), **1**, 122; *Prot. Struct. Funct. Bioinf.* (2011); **doi: 10.1002/prot.23213. [2]** E. Peter, B. Dick, S. A. Baeurle, *submitted* (2011).

BP 1.6 Mon 11:00 H 1058

Characterization of Free Energy Landscape of Villin Headpiece with Principal Components Analysis by Parts (pPCA) — •Abhinav Jain and Gerhard Stock — Biomolecular Dynamics, Institute of Physics, Albert Ludwigs University, 79104 Freiburg.

The free-energy landscape of flexible small peptides and nucleic acids can be quite complex, showing numerous metastable conformational states. On the other hand, various computational studies of proteins have given a comparatively simple picture of their energy landscape which is surprising at higher energies where the protein can reversibly fold and unfold. A method to analyze molecular dynamics (MD) simulations of protein folding is proposed, which is based on a principal component analysis (PCA) of the protein's backbone dihedral angles.[1] Adopting extensive MD simulations of the villin headpiece by Pande and co-workers [2], it is shown that "PCA by parts" allows us to characterize the free-energy landscape of the protein with unprecedented detail.

[1] Jain; Hegger; Stock. J. Phys. Chem. Lett. 2010, 1, 2769 - 2773
[2] Ensign; Kasson; Pande. J. Mol. Biol. 2007, 374, 806 - 816.

15 min break

Topical Talk BP 1.7 Mon 11:30 H 1058

Cryo electron microscopy of biological materials — •Wolfgang Baumeister — Max-Planck-Institute of Biochemistry, Martinsried, Germany

Today, essentially all electron microscopy of biological materials aiming for molecular resolution is cryo electron microscopy. Samples are examined in a frozen-hydrated state to avoid artifacts resulting from dehydration or from chemical fixation and staining. Three different imaging modalities are used: Electron crystallography, which can provide atomic resolution structures but requires that the molecules under study form well-ordered two-dimensional crystals. Single particle analysis which is the method of choice for large multi subunit protein complexes; in conjunction with other methods (hybrid methods) it can provide structures with pseudo-atomic resolution. Electron tomography allows to study large (non-repetitive) structures, such as organelles or cells, and to analyze molecular structures in situ, i.e. in their unperturbed functional environments.

In cryo electron tomography the main challenges are sample preparation and the molecular interpretation of tomograms with a poor signal-to-noise ratio. Denoising, automated segmentation, pattern recognition, and subtomogram averaging are the key strategies in tomogram interpretation. Focused ion beam technology is an emerging tool in the micromachining of frozen-hydrated samples. In conjunction with correlative fluorescence microscopy allowing the navigation of complex samples, thin lamellae suitable for tomography can be produced in a targeted manner.

BP 1.8 Mon 12:00 H 1058

Exploring protein self-diffusion in crowded solutions — •Felix Roosen-Runge[1], Marcus Hennig[1,2], Fajun Zhang[1], Robert M.J. Jacobs[3], Helmut Schober[2], Tilo Seydel[2], and Frank Schreiber[1] — [1]Institut für Angewandte Physik, Universität Tübingen — [2]ILL, Grenoble, France — [3]CRL, University of Oxford

We report a study on the self-diffusion of a globular protein, bovine serum albumin (BSA), under crowding conditions [1]. Using quasi-elastic neutron backscattering, we access the so far unexplored short-time regime of protein diffusion at nanosecond time and nanometer length scales. After separation of internal motions and rotational diffusion, the translational self-diffusion coefficients are obtained for a volume fraction range from 5% to 40%. At a biologically relevant volume fraction, the self-diffusion is slowed down by a factor of 5 compared to the dilute limit already within nanoseconds. Despite high volume fractions, no anomalous diffusion was observed at the experimental scales. Modeling the non-spherical, soft proteins with an effective hard sphere, our data agree well with predictions from colloid theory for short-time self-diffusion. This finding implies that hydrodynamic interactions are an essential part of an understanding of protein dynamics in macromolecular crowding. Comparisons are made to complementary DLS experiments [2]. The successful modeling is promising for studies on internal dynamics of proteins diffusing freely in aqueous solutions [3].

[1] F. Roosen-Runge et al., PNAS 2011, 108:11815
[2] M. Heinen et al., Soft Matter, DOI:10.1039/c1sm06242e
[3] M. Hennig et al., Soft Matter, DOI:10.1039/c1sm06609a

BP 1.9 Mon 12:15 H 1058

Solution structures and domain motions of human guanylate binding protein 1 — •Andreas Stadler[1], Adrian Syguda[2], Ralf Biehl[1], Christian Herrmann[2], and Dieter Richter[1] — [1]Forschungszentrum Jülich, ICS-1 & JCNS-1 — [2]Ruhr-Universität Bochum

Human guanylate binding protein 1 belongs to the superfamily of large GTPases. The expression of the protein in cells is strongly induced by interferons and other cytokines and it plays an important role in immune response and tumor growth. The crystal structure shows three domains: a globular head which is responsible for catalytic activity, an α-helical middle domain and a long rigid α-helical H12/H13-domain along the whole protein. The protein hydrolyses GTP to GDP and to GMP. Different conformations of the protein can be trapped during the GTP hydrolysis in solution. In the course of GTP hydrolysis, concerted large scale motions between the LG and the H12/H13 domains occur, which affect the enzymatic reaction rate.

We determined the solution structures of the protein in the different conformations during GTP hydrolysis using small angle X-ray scattering. Additionally, we measured the amplitudes and relaxation rates of the domain motions in the nm length- and 100 ns time-scale using neutron spin echo spectroscopy combined with small angle neutron scattering. The obtained results are important for a detailed understanding of the biological function of the protein on a molecular level, as we gain direct insight into the correlation of the domain motions and the enzymatic reaction.

BP 1.10 Mon 12:30 H 1058

Single-molecule fluorescence spectroscopy of the structure and dynamics of the spliceosomal complex — •Mira Prior[1], Thomas Orth[2], Peter Odenwälder[2], Ingo Gregor[1], Reinhard Lührmann[2], and Jörg Enderlein[1] — [1]Third Institute of Physics, Göttingen — [2]Max Planck Institute for Biophysical Chemistry, Göttingen

The spliceosome is the cellular machinery responsible for removing non-coding introns from precursor mRNA. During its catalytic action the spliceosome undergoes compositional and conformational changes. We are investigating the conditions for recruitment and release of particular proteins during the splicing steps. We determine how the changes occur (stepwise or in a correlated manner) and the roles of certain spliceosomal RNA helicases in the restructuring of the complex. The spectroscopic methods we use for investigating the spliceosomal complex are Dual-Focus Fluorescence Correlation Spectroscopy (2fFCS) and Dual-Color-Fluorescence Cross-Correlation Spectroscopy (2-color-FCCS). These methods allow for studying structural and dynamical properties of proteins and small nuclear ribonucleoproteins (snRNPs). 2-color-FCCS in combination with 2fFCS enables the observation of protein-protein interactions and the determination of dissociation constants for protein-protein and protein-mRNA bindings which could not be resolved with standard biochemical methods. In our experiments we focus on the B to Bact transition followed by LSm ring proteins, the thermally-stable splicing factor Cwc25 and on the proteins of the snRNP U2 complex.

BP 1.11 Mon 12:45 H 1058

Stabilization of peptide helices with respect to length and vibrational free energy — •Mariana Rossi, Volker Blum, and Matthias Scheffler — Fritz-Haber-Institut, Faradayweg 4-6, 14195 Berlin

We here address the helix-forming alanine-based Ac-Ala$_n$-LysH$^+$ polypeptide series in the gas phase, for which experiments [1] have indicated helical onset at n=8. We quantify helix stabilization wrt. peptide length and temperature [harmonic approximation for vibrational free energies (FE)], which are effects that can be dissected and accurately benchmarked in the gas phase. After an initial force-field screening, we fully relax thousands of conformers using density-functional theory with the van der Waals (vdW) corrected [2] PBE exchange-correlation potential. α-Helices are the lowest energy structures at $n \approx 7-8$ on the potential energy surface, but only barely. Interestingly, helices are systematically stabilized over globular conformers by inclusion of vibrational FE at 300K. The vibrational entropy is the leading stabilizing term at 300K, but also zero-point-energies favor helical structures by a significant amount. For $n \geq 8$, the α-helix should be the only accessible conformer in the FE surface at 300K, in agreement with experiment [1] and with our own quantitative comparison [3] of calculated *ab initio* anharmonic IR spectra to experimental IR multiphoton dissociation (IRMPD) data for Ac-Ala$_n$-LysH$^+$, n=5, 10, 15. [1] Tkatchenko and Scheffler, PRL 102, 073055 (2009); [2] Kohtani and Jarrold, JACS 108, 8454 (2004); [3] Rossi *et al.*, JPCL 1, 3465 (2010).