BP 1: Computational Biophysics (Joint Session BP/DY)

Time: Monday 9:30–13:00 Location: ZEU 250

Invited Talk BP 1.1 Mon 9:30 ZEU 250

Conformational Transitions in the Presence of Solvent and Internal Memory Effects — •Roland Netz, Julian Kappler, Jan Daldrop, Bartosz Kowalik, and Florian Brünig — Department of Physics, Free University Berlin, Arnimallee 14, 14195 Berlin, Germany

Conformational transitions of biological molecules are controlled by solvent friction. For fast transitions, such as dihedral-angle flips, the finite solvent memory time plays a role. General scaling laws for the transition time including inertial, friction and memory effects are presented. The interplay between fast molecular reconfigurations and long-time conformational relaxation and the coupling between solvent and internal friction effects is discussed.

BP 1.2 Mon 10:00 ZEU 250

Dynamics and energetics of elongation factor SelB in the ternary complex and the ribosome — •Lars V. Bock, Niels Fischer, Holger Stark, and Helmut Grubmüller — Max Planck Institute for Biophysical Chemistry, Göttingen

SelB is an elongation factor specialized to deliver the selenocysteine (Sec) tRNA to the ribosome by recoding the UGA stop codon on the mRNA. Initially the tRNA is in complex with selB and GTP forming the ternary complex (TC). High-resolution cryo-EM structures of intermediates of the Sec incorporation pathway uncover large-scale conformational changes of the ribosome and the TC. To complement the structural information with energetics and rapid dynamics, we performed extensive all-atom molecular dynamics simulations of the ribosome with bound TC as well as of the free TC in solution. The simulations of the free TC were started after extracting the TC from the ribosome-bound cryo-EM structures. The TC was found to rapidly interconvert between the different conformations allowing us to construct the free-energy landscape of the involved motions. This free-energy landscape indicates that the intrinsic large-scale conformational changes of the tRNA and SelB during the delivery to the ribosome are not rate-limiting to the process. In simulations of the free TC started from the GTPase-acitvated ribosome-bound conformation, the TC rapidly transitions into an inactivated conformation, showing that the GTPase-activated state is strongly stabilized by the ribosome. The simulations of the full ribosome with bound TC in the intermediate states allow us to identify the motions that are rate-limiting to the process of tRNA delivery and to identify the molecular mechanism of the domain closure of small ribosomal subunit upon tRNA decoding.

BP 1.3 Mon 10:15 ZEU 250

Correction of Finite-Size Effects on Diffusion in Lipid Membrane Simulations — •Martin Vögele and Gerhard Hummer — Max-Planck-Institut für Biophysik, Frankfurt am Main

Calculating diffusion coefficients from the mean squared displacement is a common task in evaluating molecular dynamics simulations. However, periodic boundary conditions introduce artifacts caused by the self-interaction with the periodic image. In cubic simulation boxes, the diffusion coefficient converges for large sizes. However, this is not the case if the system size is increased asymmetrically. [1]

We specifically test the effect of box geometry on the diffusion in lipid membranes which are usually simulated in very flat periodic boxes. There we find a logarithmic (and therefore unbounded) increase with growing box width. We discuss consequences of the apparent inability to determine a well-defined lipid diffusion coefficient from simulation and present possible methods to rationalize difficulties in comparing simulation results to each other and to experiment.

[1] M. Vögele and G. Hummer, J. Phys. Chem. B, 2016, 120 (33)

BP 1.4 Mon 10:30 ZEU 250

A Monte Carlo Study of Knots in Long Double-Stranded DNA Chains — Florian Rieger and •Peter Virnau — Johannes Gutenberg-Universität Mainz

We determine knotting probabilities and typical sizes of knots in double-stranded DNA for chains of up to half a million base pairs with computer simulations of a coarse-grained bead-stick model: Single trefoil knots and composite knots which include at least one trefoil as a prime factor are shown to be common in DNA chains exceeding 250,000 base pairs, assuming physiologically relevant salt conditions. The analysis is motivated by the emergence of DNA nanopore sequencing technology, as knots are a potential cause of erroneous nucleotide reads in nanopore sequencing devices and may severely limit read lengths in the foreseeable future. Even though our coarse-grained model is only based on experimental knotting probabilities of short DNA strands, it reproduces the correct persistence length of DNA. This indicates that knots are not only a fine gauge for structural properties, but a promising tool for the design of polymer models.

F. Rieger, P. Virnau, PLoS Comp. Biol. 12(9), e1005029 (2016).

BP 1.5 Mon 10:45 ZEU 250

Interaction of hyperbranched polyglycerol sulfate with proteins: calorimetry versus computer simulations — •Xiao Xu[1,2], Qidi Ran[3], Rainer Haag[3], Matthias Ballauff[1,2], and Joachim Dzubiella[1,2] — [1]Institut für Weiche Materie und funktionale Materialien, Helmholtz-Zentrum Berlin — [2]Institut für Physik, Humboldt-Universität zu Berlin — [3]Institut für Chemie und Biochemie, Freie Universität Berlin

Using Isothermal Titration Calorimetry (ITC) and coarse-grained (implicit solvent/explicit salt) Langevin computer simulations, we study the interaction of hyperbranched polyglycerol sulfate (hPGS) with two oppositely charged serum proteins, i.e. human serum albumin (HSA) (-) and lysozyme (+). The simulation reveals explicitly the structural properties of the complexation. We demonstrate that the driving force of the complexation in both cases originates mainly from the release of condensed counter-ions from the polymer upon binding. The binding constant fitted by single set of identical sites model shows very weak dependence on polymer size for both proteins. By applying an excluded-volume (EV) model to fit the ITC data the explict profile of binding free energy for multi-site binding between lysozyme and hPGS can be obtained. The experimental data coincides with computer simulation quantitatively especially for high generation of hPGS, which makes the simulation a useful tool to predict hPGS binding to targeted proteins such as selectins.

15 min break

BP 1.6 Mon 11:15 ZEU 250

Adsorption, binding motifs and structural change of proteins on silica studied by Molecular Dynamics — •Nils Hildebrand, Monika Michaelis, Susan Köppen, and Lucio Colombi Ciacchi — Bremen Center for Computational Materials Science, Bremen

The physisorption of chymotrypsin and lysozyme on amorphous silica is investigated by classical Molecular Dynamics (MD) methods in comparison to adsorption and circular dichroism (CD) experiments. The long-range protein-surface attraction field is calculated in an implicit solvent based on DLVO theory. These calculations reveal a preferred protein orientation, which could be confirmed in explicit solvent simulations. Driven by its large dipole moment, chymotrypsin adsorbs with its alpha-helical regions pointing towards the surface. Lysozyme adsorbs in a side-on orientation. Positively charged hydrophilic residues form dominant binding motifs by adsorbing in dense water layers around the deprotonated silanol surface groups. The amount of adsorbed proteins found in the experiment can be explained by a combination of the binding motifs stability and protein-protein interactions. No significant conformational changes are observed in MD simulations lasting 300 ns. In order to capture surface-induced conformational changes revealed by CD experiments, parallel tempering in combination with metadynamics is employed. In these simulations, the helical content of chymotrypsin is used as a reaction coordinate, as helical unfolding is believe to strengthen the adhesion to the surface.

BP 1.7 Mon 11:30 ZEU 250

Organic co-solutes in aqueous solution: The effect on local water dynamics — Johannes Zeman, Frank Uhlig, and •Jens Smiatek — Institut für Computerphysik, Universität Stuttgart, D-70569 Stuttgart, Germany

We investigate the effect of the organic co-solutes ectoine, trimethylamine N-oxide (TMAO), urea, and guanidinium chloride by means of classical and ab-initio Molecular Dynamics simulations. Our results reveal distinct effects on the local water structure and the water dy-

namics for the different co-solutes. The analysis of the diffusion coefficients and the dielectric spectra demonstrate that ectoine and TMAO significantly slow down water dynamics by a strongly bound hydration shell whereas urea and guanidinium chloride have a weaker impact. In combination with a sodium chloride solution, our findings for ectoine imply compensatory effects in order to explain the high co-solute and salt concentration in halotolerant bacteriae [1].

[1] M. B. Hahn, F. Uhlig, T. Solomun, J. Smiatek, H. Sturm; Phys. Chem. Chem. Phys. 18, 28398 (2016)

BP 1.8 Mon 11:45 ZEU 250

Determinants of nanoparticle protein corona composition investigated with molecular dynamics simulations — •Giovanni Settanni[1], Jiajia Zhuo[1], Tongchuan Suo[1], Susanne Schöttler[2,3], Katharina Landfester[2], Friederike Schmid[1], and Volker Mailänder[2,3] — [1]Department of Physics, Johannes Gutenberg University Mainz — [2]Max-Planck Institute for Polymer Research — [3]Department of Dermatology, University Medical Center Mainz

Therapeutic nanoparticles in contact with biological fluids (blood, lung surfactant, etc.) are quickly covered by a layer of proteins (corona), which determines the particle's fate in the host organism (circulation half-life, cellular uptake, tissue distribution, immune response, etc.). Nanoparticles' surfaces are often modified (adding polymer coatings, or functionalization groups etc.) to improve their therapeutic efficacy, which involve a modification of the nanoparticle protein corona composition. The molecular factors determining the corona composition of nanoparticles are not very well understood, yet. Here we use molecular dynamics simulations to investigate the non-covalent interactions taking place between several blood proteins and poly(ethylene glycol) (PEG), a hydrophilic polymer commonly used to coat nanoparticles for improved efficacies. The simulations reveal recurring patterns of interaction involving specific amino acids. The latter could be used for the development of coarse grained representations of protein-PEG interactions and may provide the basis for understanding the properties of protein coronas formed around PEGylated nanoparticles.

BP 1.9 Mon 12:00 ZEU 250

Monolayer-Protected Anionic Au Nanoparticles Walk into Lipid Membranes Step by Step — •Federica Simonelli[1], Davide Bochicchio[1], Riccardo Ferrando[2], and Giulia Rossi[1] — [1]Physics Department, University of Genoa, Via Dodecaneso 33, 16146 Genoa, Italy — [2]Chemistry Department, University of Genoa, Via Dodecaneso 31, 16146 Genoa, Italy

The design of ligand-protected metal nano-particles (NPs) with biomedical applications relies on the understanding, at the molecular level, of their interactions with cell membranes. We study, via unbiased coarse grained molecular dynamics simulations, the kinetics and the thermodynamics of the interaction between anionic ligand-protected gold NPs and model lipid membranes. We find that the NP-membrane interaction is a three-step process: electrostatics-driven adhesion to the membrane surface, hydrophobic contact and final embedding in the membrane core via anchoring of the charged ligands to both membrane leaflets. Our free energy calculations show that anchoring is highly favorable and not reversible. Furthermore, the interaction pathway of NPs with random surface arrangement of anionic and hydrophobic ligands is characterized by two metastable configurations: adsorbed at the membrane surface, and membrane-embedded. Patched ligand arrangements, instead, lead to the stabilization of a third, intermediate metastable configuration, resulting in a much slower kinetics of interaction with the membrane.

BP 1.10 Mon 12:15 ZEU 250

Modeling epidemic patterns of multiple diseases with short-term non-specific immunity — •Gorm Gruner Jensen[1], Florian Uekermann[1], Kim Sneppen[1], and Lone Simonsen[2] — [1]Niels Bohr Institute, University of Copenhagen, Blegdamsvej 17, Copenhagen 2100-DK, Denmark — [2]Department of public health, University of Copenhagen, Øster Farimagsgade 5, Copenhagen 1014-DK, Denmark

A number of common respiratory viruses cause seasonal epidemics in a particular sequential pattern. Seasonal drivers like reduced immune function in mid-winter have been proposed as a possible cause. While these drivers may be sufficient to explain mid-winter viruses such as influenza, it is not clear whether other viruses require different drivers to explain their occurrence in spring, summer or fall. Here we use a multi-disease model to explore the possibility that a short non-specific immunity explains their seasonal patterns as a consequence of interaction between the diseases rather than requiring multiple seasonal drivers or complex pairwise interaction.

In the presence of a single seasonal driver, working identically on all diseases, our model exhibits a variety of observed epidemic patterns, including ordered peaks of different diseases. As example for application to observed patterns, we show two disease simulations reproducing multiple features of the correlation between annual PIV-3 and biennial PIV-1 epidemic peaks.

BP 1.11 Mon 12:30 ZEU 250

Characterization of coarse-grained helix-coil transition networks — •Joseph Rudzinski, Kurt Kremer, and Tristan Bereau — Max Planck Institute for Polymer Research, Ackermannweg 10, 55128 Mainz, Germany

A variety of models, with widely-varying resolution, have contributed to our interpretation of the protein folding process. While atomically-detailed simulations have emerged as an invaluable tool for describing the subtle details which determine particular folding processes, simple physics- and native structure-based coarse-grained (CG) models laid the foundation for current protein folding theories. Despite the success of the latter in describing the essential features of protein folding, the reduced degrees of freedom in CG models inherently obscures the resulting dynamical properties, generally limiting their utility. In this work, we investigate to what extent CG models can describe the precise network of transition pathways for particular protein folding processes. As a model system, we consider the well-studied problem of helix-coil transition kinetics. To elucidate the generic features of the transition, while retaining an accurate description of the transition pathways, we consider a hybrid model with simple, physically-motivated interactions coupled with atomically-detailed sterics. We compare the resulting transition network to networks generated from both an all-atom model and a more sophisticated, transferable CG model. Our results indicate that many features of the transition network are prescribed by rather generic features of the model, motivating further investigation of protein folding kinetics using this approach.

BP 1.12 Mon 12:45 ZEU 250

Mechanism of rhomboid intramembrane proteolysis — •Ana Nicoleta Bondar — Department of Physics, Freie Universität Berlin, Arnimallee 14, D-14195 Berlin, Germany

Intramembrane proteases are membrane-embedded proteins whose substrates are transmembrane protein segments. Reaction mechanisms of intramembrane proteases are important to understand, because these proteins are implicated in essential processes such as cell signalling. A fundamental open question is how specific lipid molecules participate in the reaction coordinate of intramembrane protease. We address this question with extensive all-atom molecular dynamics simulations of the intramembrane rhomboid protease from Escherichia coli, GlpG. The computations indicate coupling between lipid binding at the substrate docking-site region and the composition of the lipid membrane, highlighting the importance of lipid interactions for the reaction coordinate of the protease.

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References

1. A.-N. Bondar. Biophysical mechanism of rhomboid proteolysis: setting a foundation for therapeutics. Seminars in Cell and Developmental Biology 10.1016/j.semcdb.2016.09.006, Accepted (2016).

2. A.-N. Bondar, C. del Val, and S. H. White. Rhomboid protease dynamics and lipid interactions. Structure 17: 395-405 (2009).