BP 8: Posters: Proteins

Time: Monday 17:30–19:30 Location: Poster B2

BP 8.1 Mon 17:30 Poster B2

Effects of ligand binding on cyclophilin A: experimental and computational studies — •Jack Heal[1], Stephen Wells[2], Claudia Blindauer[3], Rudolf Römer[2], and Robert Freedman[4] — [1]MOAC Doctoral Training Center, University of Warwick, Coventry, UK, CV4 7AL — [2]Department of Physics, University of Warwick, Coventry, UK, CV4 7AL — [3]Department of Chemistry, University of Warwick, Coventry, UK, CV4 7AL — [4]Department of Life Sciences, University of Warwick, Coventry, UK, CV4 7AL

Cyclophilin A is an enzyme which plays a role in the folding of proteins. It also binds to and aids the function of the immunosuppressant drug cyclosporin A as well as binding to the HIV-1 capsid protein. We use the computational tools FIRST and FRODA to model the flexibility and motion of cyclophilin A in order to predict the results of hydrogen-deuterium exchange NMR (HDX) experiments. The rigidity analysis software FIRST can be used to predict the 'folding cores' of proteins identified as slowly exchanging residues in HDX. This prediction is improved using the protein mobility software FRODA. We are using these methods to investigate the effect of ligand binding on cyclophilin A computationally and experimentally.

BP 8.2 Mon 17:30 Poster B2

Peptide interactions with metal surfaces — •Isidro Lorenzo[1], Hendrik Heinz[2], and Marialore Sulpizi[1] — [1]Johannes Gutenberg University Mainz, Staudinger Weg 7 55099 Mainz — [2]Departament of Polymer Engineering, University of Akron, Ohio 44325

Understanding and controlling protein-surface interactions is gaining increasing fundamental scientific interest, such as in medical, diagnostic and biotechnology applications.

In this work we want to provide a characterization of peptide / gold interactions at a molecular level in order to explain and interpret recent surface experiments [1].

Atomistic simulations have been performed with the GROMACS package using available force field parameters such as CHARMM27 using 12-6 Lennard-Jones potentials [2] force field. We have employed a recently developed force field which has been extensively tested in biomolecular-inorganic interactions [3]. This has permitted to identify the most favorable binding modes on the different surfaces. Both neutral and zwitterionic forms for each peptide are analyzed .

[1] Anne Vallee, Vincent Humblot, and Claire-Marie Pradier Acc. Chem. Res., 2010, 43 (10), pp 1297*1306

[2] Heinz H, Vaia RA, Farmer BL, Naik RR J. Phys. Chem. C 2008, 112, 17281 17290

[3] Heinz H, Farmer BL, Pandey RB, Slocik JM, Patnaik SS, Pachter R, Naik RR. J. Am. Chem. Soc. 2009, 131, 9704-9714

BP 8.3 Mon 17:30 Poster B2

Time-Resolved FTIR Difference Spectroscopy of Vibrational Control Experiments on Bacteriorhodopsin — •Christian Bauer[1,2], Michael Gensch[2], and Joachim Heberle[1] — [1]Freie Universität Berlin — [2]HZDR

We aim at investigating how photoreactions of proteins can be controlled by means of intense THz radiation tuned in resonance to specific vibrational modes, much in analogy to coherent control experiments conducted by fs NIR laser pulses [1]. Bacteriorhodopsin is the sole protein of the purple membrane of the archaebacterium Halobacterium salinarum [2]. Upon illumination, its chromophore retinal isomerizes around the C13-C14 double bond [3] and the protein undergoes a sequence of intermediate states which is called a photocycle. For investigation of this photocycle we combined a time-resolved IR difference spectroscopic setup using the step-scan technique [4] with intense, tunable narrow bandwidth THz radiation at the ps beamline of the THz free electron laser FELBE [5]. In our experiments, the photoreaction is initiated by a visible laser pulse as in standard experiments, but then the sample will be irradiated by a THz pulse from the free electron laser tuned into resonance with low-energy vibrational modes which is supposed to influence the photoreaction [1].

[1] Prokhorenko V.I. et al. Science 313, 1257 (2006) [2] Oesterhelt D. et al. PNAS 70, 2853 (1973) [3] Stoeckenius W. et al. Biophys. Struct. Mech. 3, 65 (1977) [4] Radu I. et al. Photochem. Photobiol. Sci. 8, 1517 (2009) [5] Bauer, C. et al. Journal of Physics Conference Series, 359, 012011 (2012)

BP 8.4 Mon 17:30 Poster B2

Dual-Color Fluorescence Cross-Correlation Spectroscopy of the macromolecular spliceosomal complex — •Mira Prior[1], Thomas Ohrt[2], Julia Dannenberg[2], Ingo Gregor[1], Reinhard Lührmann[2], and Jörg Enderlein[1] — [1]Drittes Physikalisches Institut-Biophysik, Göttingen — [2]Max Planck Institut für Biophysikalische Chemie, 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 method we use is Dual-Color-Fluorescence Cross-Correlation Spectroscopy (2-color-FCCS) which allows for studying structural and dynamical properties of proteins. We observed the thermally stable splicing factor Cwc25. We could determine, under which conditions it binds to the complex, when it is released and the conditions for stable binding of Cwc25 to the spliceosome. By measuring several mutants we could answer the question whether Cwc25 is released before or during the second catalytic step. Furthermore, we detected the binding of the proteins Slu7 and Prp16. These proteins are necessary for the second catalytic step and are involved in the binding behavior of Cwc25.

BP 8.5 Mon 17:30 Poster B2

Tip-Enhanced Raman Spectroscopy on Membrane Proteins — •Elmar Hassan Hubrich and Joachim Heberle — Freie Universität Berlin, Department of Physics, Exp. Molecular Biophysics, Arnimallee 14, 14195 Berlin, Germany

Membrane proteins are essential parts of organisms and involved in cell processes such as transport, signal transmission, catalysis, cell adhesion and (photo-)synthese. Obtaining information on molecular level of such proteins is one of the major tasks in modern biophysics.

In these research, we attempt to develop tip-enhanced Raman spectroscopy (TERS), as a tool to study structure and function of single proteins. TERS combines high spatial resolution of AFM with structural sensitivity of surface-enhanced Raman spectroscopy (SERS). Using a gold-coated AFM tip, it is possible to measure Raman signals with a spatial resolution up to 20 nm.

Additionally to imaging a SERS probe (=TERS), AFM can be used induce and messure physical force. The force is used to achieve structural changes or even unfolding of a protein, namely single-molecule force spectroscopy (SMFS).

SERS can be used to achieve molecular level information while AFM applies a physical force. In order to detect single proteins we use the enhancement of SERS. The Raman signal is enhanced in the vicinity of silver- or gold-coated surfaces (here: the AFM tip).

Up to now, this technique is mainly applied to inorganic samples. Here, we introduce the experimental setup and discuss the application of TERS to the investigation of membrane proteins.

BP 8.6 Mon 17:30 Poster B2

Dynamic force spectroscopy on the binding of monoclonal antibodies to tau peptides — •Carolin Wagner[1], David Singer[2], Tim Stangner[1], Christof Gutsche[1], Ralf Hoffmann[2], and Friedrich Kremer[1] — [1]Leipzig University, Department of Molecular Physics, Leipzig, Germany — [2]Leipzig University, Institute for Bioanalytical Chemistry, Leipzig, Germany

Optical tweezers-assisted dynamic force spectroscopy (DFS) is employed to investigate specific receptor/ligand bindings on the level of single binding events [1]. Here, the binding of the phosphorylation-specific antibody HPT-101, to synthetic tau-peptides with two potential phosphorylation sites (Thr231 and Ser235) is analyzed. According to ELISA-measurements, the antibody binds only specificly to the double-phosphorylated tau-peptide. It is shown by DFS that HPT-101 binds also to each sort of the mono-phosphorylated peptides. By analyzing the measured rupture-force distributions characteristic parameters like the lifetime of the bond without force, the characteristic length and the free energy of activation are determined for all interactions. The longest lifetime is obtained for the specific binding to the

double-phosphorylated peptide. Furthermore we introduce a method to estimate the relative affinity of the bonds from dynamic single-molecule experiments. The result is in accordance with the ELISA measurements.

[1] C. Wagner et al., Soft Matter, 2011, 7 (9), 4370 - 4378

BP 8.7 Mon 17:30 Poster B2

Hydrophobin adsorption to the air/water interface: Unusual adsorption kinetics and their origin — •Jonas Raphael Heppe[1], Sebastian Backes[1], Hendrik Hähl[1,2], and Karin Jacobs[1] — [1]Saarland University, Experimental Physics, 66041 Saarbrücken, Germany — [2]University of Zurich, Institute of Physical Chemistry, 8057 Zürich, Switzerland

Adsorption of proteins to the interface between water and other liquids (e.g. oil) or air is of major technological interest. Adsorbed proteins stabilize this interface and hence serve as emulsifying or foaming agent. In food industry, this characteristic is used for products such as milk, beer, or coffee. To optimize production sequences and to be able to give predictions, a deeper understanding of the competitive processes leading to the final adsorbate is necessary. Hydrophobins are a class of proteins that have emerged to have a high technological potential and may also serve as ideal model candidates. Produced by filamentous fungi, hydrophobins are extremely conformationally stable, particularly amphiphilic, highly surface active, and form ordered layers at the water surface [1,2]. We studied wild types and specifically designed mutants of hydrophobins featuring different properties, sizes, and forms. To access the processes involved in the adsorption, we used ellipsometry to record in situ the adsorbed amount at different ambient and solution conditions. Our results reveal adsorption kinetics that significantly differ from that of other systems and cannot be explained by conventional theoretical models. [1] S. Varjonen et al., Soft Matter 7 (2011) 2402 [2] T. Hakala et al., RSC Advances 2 (2012) 9867

BP 8.8 Mon 17:30 Poster B2

Demonstration of catch bonds between glycosaminoglycan and positively charged hydrophilic domain from the cell surface sulfatase Sulf1 — •A.-K. Möller, A. Harder, F. Milz, P. Neuhaus, V. Walhorn, Th. Dierks, and D. Anselmetti — Bielefeld University, Germany

The unique hydrophilic domain (HD) found in the human sulfatases Sulf1 and Sulf2 is responsible for targeting Sulf1 to the cell surface by interacting with its substrate. The enzymatic activity of Sulf1 is known to be specifically directed towards the 6-O-sulfation sites of heparan sulfate (HS) within highly sulfated regions of the glycosaminoglycan. Since the function of many growth and differentiation factors is regulated by HS, which acts as an essential cofactor for the interaction with cell surface localized receptors, these molecular and cellular interactions have great influence on embryogenesis and homeostasis. We used single-molecule AFM force spectroscopy (SMFS) to investigate the specificity of the interaction between HD and the glycosaminoglycans dermatan sulfate (DS) as well as heparin (Hep), the latter serving as model for the interacting regions of HS due to its high sulfation. Thereby we found an increased binding probability by increasing pulling velocity which is similar to experiments on P-selectin and its counterligand PSGL-1. We additionally applied AFM force clamp experiments to measure the force-dependent lifetimes of the interaction. We observed prolonged bond lifetimes under higher tensile forces between 10-20 pN, which we will discuss within the framework of molecular catch bonds.

BP 8.9 Mon 17:30 Poster B2

Investigation of enzyme complex dynamics via atomic force microscopy — •Mitja Platen[1], Sabin Prajapati[2], Kathrin Schröder-Tittmann[2], Kai Tittmann[2], and Iwan Schaap[1] — [1]III. Physikalisches Institut, Georg August Universität Göttingen, Germany — [2]Albrecht-von-Haller-Institut, Georg August Universität Göttingen, Germany

The pyruvate dehydrogenase multienzyme complex (PDHc) links glycolysis to the citric acid cycle by converting central metabolite pyruvate into acetyl-CoA, a building block for many fundamental metabolic pathways. The core of the human PDHc consists of 60 dihydrolipoamide acetyltransferase enzymes (E2), which assemble into a 50 nm diameter dodecahedral structure. A key trait vital to PDHc function is the flexibility of the N-terminal "swinging lipoyl domain" of E2, which is capable of reaching the active sites of all proximal enzyme components. Although low resolution structural information about the PDHc is available, the underlying dynamics of catalysis, in particular substrate channeling, is not understood.

To be able to observe the structure of single PDH complexes we are applying AFM in liquid. Ultimately, we aim to observe the core dynamics at real-time via optimization of imaging techniques by exploring the limits of amplitude and frequency modulation as well as jumping mode AFM. We will present our approach to maximize the spatial and temporal resolution and will present our first results on this enzyme complex.

BP 8.10 Mon 17:30 Poster B2

Self-diffusion of proteins in solution close to a salt-induced phase transition — •Marco Grimaldo.[1], Vincent Glenisson[1,2], Marcus Hennig[1], Felix Roosen-Runge[1], Fajun Zhang[1], Tilo Seydel[2], and Frank Schreiber[1] — [1]Fakultät für Physik - Universität Tübingen, Auf der Morgenstelle 10, D-72076 Tübingen, Germany — [2]Institut Laue-Langevin, B.P. 156, F-38042 Grenoble, France

A reentrant phase diagram is observed in aqueous solutions of Bovine Serum Albumin (BSA) upon addition of a trivalent salt (Yttrium Chloride) at concentration c_s . In particular, increasing c_s for a certain protein concentration c_p, a phase transition occurs at a characteristic concentration c_s^*. For $c_s > c_s^*$ macroscopic aggregates form [1]. Measurements on the neutron backscattering spectrometers IN10 and IN16 at the Institute Laue-Langevin have shown that the short time self-diffusion of the proteins in such system decreases when c_s approaches c_s^*. For a better understanding of this phenomenon, data has been collected also with the backscattering spectrometer BASIS (SNS, ORNL) in order to increase the accessible time scales. In presenting the data analysis we will also discuss the method adopted to obtain consistent results from different quasi-elastic neutron scattering (QENS) instruments.

[1] Zhang et al. PRL 101 (2008) 148101
[2] Roosen-Runge et al. PNAS 108 (2011) 11815

BP 8.11 Mon 17:30 Poster B2

Biophysical Characterization of the Platelet Factor 4-Heparin Complex Responsible for Heparin-induced Thrombocytopenia — •Martin Kreimann[1], Werner Weitschies[2], Andreas Greinacher[3], and Mihaela Delcea[1] — [1]ZIK HIKE, University of Greifswald, Greifswald, Germany — [2]Department of Biopharmaceutics and Pharmaceutical Technology, University of Greifswald, Greifswald, Germany — [3]Institute for Immunology and Transfusion Medicine, University of Greifswald, Greifswald, Germany

The human protein Platelet Factor 4 is known to form complexes with the polysaccharide heparin when the latter is administered as an anticoagulant during cardiac surgery. This complex is responsible for the fatal adverse effect known as heparin-induced thrombocytopenia. The study of the PF4-heparin complex is primordial because heparin remains one of the most frequently used anticoagulants. To determine the biophysical basis of the PF4-heparin complexes, the binding interaction between PF4 and heparin was investigated by Isothermal Titration Calorimetry and Quartz Crystal Microbalance and the formed complexes were imaged by Atomic Force Microscopy. Our data shows that the binding of PF4 to heparin is mainly driven by electrostatic interactions. Hydrophobic interactions and conformational restrictions only play a minor role in the energetics of the process. AFM imaging shows that the height of PF4 molecules appearing as single features is reduced when complexed with heparin.

BP 8.12 Mon 17:30 Poster B2

The dynamics and flexibility of protein disulphide-isomerase (PDI): simulations predict experimentally-observed domain motions — J Emilio Jimenez-Roldan[1], Moitrayee Bhattacharyya[2], Stephen A Wells[1], •Rudolf A Römer[1,4], Saraswathi Vishweshwara[2], and Robert B Freedman[3] — [1]Department of Physics, The University of Warwick, Coventry, UK — [2]Department of Biochemistry, IISc, Bangalore, India — [3]School of Life Sciences, The University of Warwick, Coventry, UK — [4]Centre for Scientific Computing, The University of Warwick, Coventry, UK

We simulated the mobility of the folding catalyst, protein disulphide-isomerase (PDI), by molecular dynamics and by a rapid approach based on flexibility analysis. We analysed our simulations using measures of backbone movement, relative positions and orientations of domains, and distances between functional sites. Despite their different assumptions, the two methods are surprisingly consistent. Both methods show that motion of domains is dominated by hinge and rotation motion of the a and a' domains relative to the central b-b' domain core. Both methods identify the a' domain as showing the greatest

intra-domain mobility. However, only the flexibility method, which requires 10^4-fold less computer power, predicts some large-scale features of inter-domain motion that have been observed experimentally. We conclude that the methods provide complementary insight into the motion of this large protein and detailed structural models that characterise its functionally-significant conformational changes.

BP 8.13 Mon 17:30 Poster B2

Proteinfoldingdynamics of hPin1 WW domain studied by single molecule FRET. — •Phillip Kroehn and Jörg Enderlein — Universität Göttingen, Deutschland

Georg-August-Universität Göttingen, Friedrich-Hundt-Platz 1, 37077 Göttingen

Förster resonance energy transfer (FRET) is the commonly used method to study fast molecular dynamics in a scale of 1-10 nanometer.

The energy transfer between a donor molecule and an acceptor molecule e.g. organic fluorophore by dipole interaction depends strongly on the distance between them.This phenomenon offers the possibility to use FRET as a nonoscopic ruler.

The primary structure of small soluble proteins is believed to contain all chemical information necessary for proper folding to its native state.The hPin1 WW Domain is a 40 Amino acid all beta sheet protein that consist of three strands. It can be seen as a simple model system to investigate the formation of beta fold secondary structures.

The hPin1 is involved in cell cycle regulation, the WW domain at the N terminal site of hPin1 is able to bind to proline rich ligands. Due to its high thermal stability the hPin1 WW domain is suitable for folding/unfolding studies.

BP 8.14 Mon 17:30 Poster B2

Reaction mechanism of the enzyme PHM: quantum tunneling and origin of kinetic isotope effects — •Enrique Abad, Judith Rommel, and Johannes Kästner — Computational Biochemistry Group, Institut für Theoretische Chemie, Universität Stuttgart, Stuttgart, Germany

Copper proteins catalyze important biochemical reactions, in particular in the nervous system of higher eukaryotes. PHM is a binuclear Cu protein that stereospecifically hydroxylates one C-H bond of small peptides (such as oxytocin), as a intermediate step for its later amidation.

The reaction mechanism of PHM is still not understood. Several proposals have been made [1, 2], but they have not taken explicitly into account the strong kinetic isotope effects (KIE) present in this reaction [3]. In this work, we perform QM/MM calculations at the DFT level, and tunneling rates for a set of possible reaction paths. We suggest a new reaction mechanism in which tunneling of a H atom is crucial for explaining the KIE.

[1] A. Crespo, et al. (2006) J. Am. Chem. Soc. 128, 12817
[2] P. Chen and E. I. Solomon (2004) J. Am. Chem. Soc. 126, 4991
[3] W. A. Francisco, et al. (2002) J. Am. Chem. Soc. 124, 8194

BP 8.15 Mon 17:30 Poster B2

Intracellular crowding effects on cellular metabolism — •Florencia Noriega[1], Márcio Argollo[2], and Alexei Vázquez[3] — [1]MPI for Dynamics and Self-Organization, Göttingen, Germany — [2]UFF, Niterói, Brazil — [3]UMDNJ-Robert Wood Johnson Medical School, New Brunswick, USA

70 to 90% of the dry weight in the cell is occupied by the 3 types of macromolecules: DNA, RNA and proteins. The high density levels of macromolecular components in the cellular cytoplasm, also known as molecular crowding, is important for the development of many cellular functions like protein folding, protein protein association and dissociation, biochemical reactions rates, molecular diffusion within the cell, among others. It has been shown that molecular crowding acts also at a global scale limiting the cytoplasm solvent capacity [1], due to the limited available volume in the cell. To estimate the molecular crowding global effect on a simple cellular metabolic network we develop a flux balance model considering the macromolecular concentrations at different growth rates and determine the metabolic steady states, given by the fluxes of the metabolic reactions. We found a metabolic switch, activation and inactivation of the fluxes, in a simple cell model, when is shifted from low to high growth rates. Such behavior is observed in yeast cells and is called crabtree effect, where at high growth rates acetate compound is secreted by the cell, indicating the activation of the fermentation pathway of glucose consumption.

[1] Beg QK, et al.(2007) PNAS 104: 12663-12668. Vázquez A, et al. (2008) BMC Systems Biol 2: 7.

BP 8.16 Mon 17:30 Poster B2

Robust signatures in the current-voltage characteristics of DNA molecules oriented between two graphene nanoribbon electrodes — Carlos J. Paez[1], Peter A. Schulz[1,2], Neil Wilson[3], and •Rudolf A. Römer[3,4] — [1]Instituto de Fisica Gleb Wataghin, Universidade Estadual de Campinas, 777 Cidade Universitaria 13083-859 Campinas, SP Brazil — [2]Faculdade de Ciencias Aplicadas, Universidade Estadual de Campinas, 13484-350 Limeira, SP Brazil — [3]Department of Physics, University of Warwick, Coventry, CV4 7AL, UK — [4]Centre for Scientific Computing, University of Warwick, Coventry, CV4 7AL, United Kingdom

In this work we numerically calculate the electric current through three kinds of DNA sequences (telomeric, λ-DNA, and p53-DNA) described by different heuristic models. A bias voltage is applied between two zig-zag edged graphene contacts attached to the DNA segments, while a gate terminal modulates the conductance of the molecule. We show that a telomeric DNA sequence, when treated as a quantum wire in the fully coherent low-temperature regime, works as an excellent semiconductor. Clear steps are apparent in the current-voltage curves of telomeric sequences and are present independent of lengths and sequence initialisation at the contacts. independent of length and sequencing initialisation at the contacts. The difference between telomeric DNA and other DNA, such as λ-DNA and DNA for the tumour suppressor p53, is particularly visible in the length dependence of the current.

BP 8.17 Mon 17:30 Poster B2

Video-based and interference-free axial force detection and analysis for optical tweezers — •Sebastian Knust, Andre Spiering, Andy Sischka, and Dario Anselmetti — Experimental Biophysics & Applied Nanoscience, Faculty of Physics, Bielefeld University, 33615 Bielefeld, Germany

For measuring the minute forces exerted on single molecules during controlled translocation through nanopores with sub-piconewton precision, we have developed a video-based axial force detection and analysis system for optical tweezers [1].

As the bandwidth of the system is not as high as in backscattered light based systems, we integrated Allan variance analysis [2] for trap stiffness calibration.

Upon manipulating a microbead in the vicinity of a weakly reflecting surface with simultaneous axial force detection, interference effects have to be considered [3]. We measured and analyzed the backscattering light properties of polystyrene and silica microbeads with different diameters and propose distinct and optimized experimental configurations (microbead material and diameter) for minimal light backscattering and virtually interference-free microbead position detection.

As a proof of principle, we investigated the nanopore threading forces of a single dsDNA strand attached to a microbead with an overall force resolution of ± 0.5 pN at a sample rate of 123 Hz.

[1] S. Knust et. al., Rev. Sci. Instrum. **83**, 103704 (2012)
[2] B. Lansdorp, O. Saleh, Rev. Sci. Instrum. **83**, 025115 (2012)
[3] A. Sischka et. al., Rev. Sci. Instrum. **79**, 63702 (2008)

BP 8.18 Mon 17:30 Poster B2

Mechanical properties of sister chromatids studied by a polymer model — •Sebastian Isbaner, Yang Zhang, and Dieter W. Heermann — Institute for Theoretical Physics, Heidelberg University, Germany

A chromosome in metaphase consists of two highly condensed sister chromatids forming a chromosome. In experiments, chromosomes show characteristic force-extension curves with a linear region followed by a plateau. However, where and how exactly sister chromatids are linked to each other and how these links influence their overall organization and mechanical properties is still not well understood. In this work, we use a dynamic folding model for mitotic chromatids and investigate the influence of dynamic cross-links between two model sister chromatids. Our results show that the number of sister links has severe influence on the overall organization of the model chromatids. Too few cross-links cause the model chromatids to drift apart due to entropic repulsion, whereas many links result in an agglomeration. We characterize these different states in a phase diagram. We further investigate the force-extension behavior and find that it qualitatively reproduces experimental results. Our results also demonstrate that inter sister cross-links decrease the elasticity compared to isolated model chromatids. In summary, we show that only a limited range for the

concentration of inter sister chromatid cross-links can exist to result in observed chromosome shapes and our model is able to reproduce experimental findings for the elasticity of chromosomes.

BP 8.19 Mon 17:30 Poster B2

Computational Analysis of Co-transcriptional Riboswitch Folding — •Benjamin Lutz[1,2], Abhinav Verma[1], and Alexander Schug[1] — [1]Steinbuch Centre for Computing (SCC), Karlsruher Institut für Technologie (KIT), 76128 Karlsuhe, Germany — [2]Fakultät für Physik, Karlsruher Institut für Technologie (KIT), 76128 Karlsruhe, Germany

Structured RNA in non-coding regions often plays crucial regulatory roles. Riboswitches are an important example that can prevent expression of the downstream gene by terminating transcription or translation. Typically, one out of two distinct conformations is formed depending on ligand binding. The extrusion out of RNA polymerase (RNAP) takes place at time scales comparable to those of folding and binding. We investigate these interdependent processes by simulating the extrusion out of RNAP and concurrent folding for the SAM-I and adenine riboswitches with molecular dynamics. Atomically resolved structure-based models reduce the computational effort sufficiently to simulate different extrusion velocity scenarios. Depending on the scenario, we observe and quantify different pathways in structural formation. Considering the inherent link of folding and binding, this underlines modulation of extrusion velocity as another degree of freedom in genetic evolution. Our simulational findings therefore complement experimental measurements to understand the dynamic behavior of nascent RNA.

BP 8.20 Mon 17:30 Poster B2

Ubiquitin dynamics in complexes investigated using Molecular Dynamics simulations — •Jan Henning Peters and Bert de Groot — Max Planck lnstitute für Biophysikalische Chemie, Göttingen, Germany

Protein-protein interactions play an important role in all biological processes. However, the principles underlying these interactions are only beginning to be understood. Ubiquitin is a small signalling protein that is covalently attached to different proteins to mark them for degradation, regulates transport and other functions. As such, it interacts with and is recognised by a multitude of other proteins. We have conducted molecular dynamics simulations of ubiquitin in complex with several different binding partners on a microsecond timescale and compared them with ensembles of unbound ubiquitin to investigate the principles of their interaction and determine the influence of complex formation on the dynamic properties of this protein. Along the main mode of fluctuation of ubiquitin, binding in most cases reduces the conformational space available to ubiquitin to a subspace of that covered by unbound ubiquitin. This behaviour can be well explained using the model of conformational selection. For lower amplitude collective modes, a spectrum of zero to almost complete coverage of bound by unbound ensembles was observed. The significant differences between bound and unbound structures are exclusively situated at the binding interface.

BP 8.21 Mon 17:30 Poster B2

Discerning overall and internal motion of flexible molecules — •Florian Sittel and Gerhard Stock — University of Freiburg

Classical molecular dynamics (MD) simulations allow us to study the structure and dynamics of biomolecules in microscopic detail. To extract the internal molecular motion from an MD trajectory, first the overall motion of the molecule needs to be removed. This procedure is well established in the case that the molecule is almost rigid, i.e. if the vibrational dynamics is well described by small-amplitude motion around an equilibrium structure. In the case of a flexible molecule, however, the transformation does not completely decouple internal and rotational motion due to rotovibrational coupling. In this work, we study the range of validity and applicability of commonly used rotational fitting techniques. To this end, we adopt previously performed MD simulations of polyalanine and villin and compare their conformational distribution in internal and Cartesian coordinates. The study reveals that the free energy landscape of a Cartesian PCA can exhibit remarkable artifacts. Cartesian coordinates on the other hand, may be superior for the study of small-amplitude functional motions in proteins.

BP 8.22 Mon 17:30 Poster B2

Langevin simulations of proteins using models in generalized coordinates — •Sina Zendehroud, Anne Müller, and Martin E. Garcia — Theoretische Physik, Fachbereich 10, Universität Kassel. Kassel, Germany

Using the the coarse-grained protein model developed by Nan-Yow Chen et al. [Phys. Rev. Lett. 96, 078103 (2006)], we derived the Langevin equation of motion in generalized coordinates, namely the Ramachandran angles. We developed a code to integrate the aforementioned equation for small real proteins. The interaction potential does not need any a priori information about the native conformation. We have studied the folding behavior of different proteins.

BP 8.23 Mon 17:30 Poster B2

Langevin simulations of conformational changes in proteins under non-equilibrium conditions — •Anne Müller, Bernhard Reuter, and Martin E. Garcia — Theoretische Physik, Universität Kassel, Fachbereich 10, Kassel, Germany

Using the potential of a coarse-grained model of proteins developed by Nan-Yow Chen et al. [PhysRevLett.96.078103(2006)], we developed a program to simulate the folding dynamics of small, real proteins through integration of the Langevin equation of motion. The force field does not need any a priori information about the native state and is known to be able to describe the folding of proteins to both alpha-helices and beta-sheets. We have studied the folding behavior of proteins which present both secondary structures in their native state. In particular we investigated the influence of temperature gradients on the dynamics of the proteins during conformational changes.

BP 8.24 Mon 17:30 Poster B2

Adjusting a Langevin model to Molecular Dynamics — •Norbert Schaudinnus[1], Andrzej Rzepiela[1], Rainer Hegger[2], and Gerhard Stock[1] — [1]Biomolecular Dynamics, Physikalisches Institut, Universität Freiburg, Hermann-Herder-Str. 3, 79104 Freibur — [2]J.W. Goethe University, Institute for Physical and Theoretical Chemistry, Max-von-Laue-Str. 7, 60438 Frankfurt/Main

Molecular Dynamics simulations (MD) are nowadays routinely used to investigate the behaviour of proteins, employing huge amounts of resources to propagate the Newtonian equations of motion for each atom. The Langevin formalism provides a method to recover those dynamics, based on a reduced subset of collective coordinates. Describing the time evolution as a superposition of drift and diffusive motion, the Langevin approach has been shown to correctly reproduce the conformational dynamics of polyalanines [1]. Using local estimates to compute the corresponding fields from MD trajectories, the method contains parameters, which determine the accuracy of the Langevin approach. We investigate this dependence providing a strategy to optimize the Langevin technique. We further demonstrate a method to reduce the amount of underlying data used to compute our estimates in a reliable way to further increase the efficiency of our method. We show the application of our method for various peptide systems. [1] R. Hegger and G. Stock, J. Chem. Phys. 130, 034106 (2009)

BP 8.25 Mon 17:30 Poster B2

Thermal, Autonomous Replicator Made from Transfer RNA — Hubert Krammer, •Friederike M. Möller, and Dieter Braun — Systems Biophysics, Physics Department, Center for Nanoscience, Ludwig Maximilians Universität München, Amalienstrasse 54, 80799 München, Germany

Evolving systems rely on the storage and replication of genetic information. Here we present an autonomous, purely thermally driven replication mechanism. A pool of hairpin molecules, derived from transfer RNA replicates the succession of a two-letter code. Energy is first stored thermally in metastable hairpins. Thereafter, energy is released by a highly specific and exponential replication with a duplication time of 30 s, which is much faster than the tendency to produce false positives in the absence of template. Our experiments propose a physical rather than a chemical scenario for the autonomous replication of protein encoding information in a disequilibrium setting.

BP 8.26 Mon 17:30 Poster B2

Analyzing protein folding by high-throughput simulations — •Claude Sinner[1,2], Benjamin Lutz[1,2], Abhinav Verma[1], and Alexander Schug[1] — [1]Steinbuch Centre for Computing (SCC),Karlsruher Institut für Technologie (KIT), 76128 Karlsuhe, Germany — [2]Fakultät für Physik, Karlsruher Institut für Technologie (KIT), 76128 Karlsruhe, Germany

Molecular Dynamics allows investigating the dynamical properties

of biomolecules. Protein folding simulations are computationally challenging when simulating all involved (solvent) atoms considering timescales of ms or slower. Native structure based models (SBM,'Go-models') reduce computational complexity and have shown to be a robust and efficient way for exploring the protein folding process. They are based on energy landscape theory and the principle of minimal frustration. Using this framework, we simulate protein folding for a large set ($\sim$ 200) of non-homologous monomeric proteins sized from 50-150 amino acids in coarse-grained simulations. A fully automatized workflow implemented with the help of $_{\mathrm{E}}$SBMTools guides these simulations. From the simulations, we extract typical folding properties like phi-values, folding free energy landscape and transition state ensembles. We repeat the simulations for a variant SBM with flavored contact strengths pending on amino acid composition. The resulting database estimates the robustness of folding parameters, quantifies the folding behavior, compares the behavior to existing experimental data and can serve as a baseline for comparison to future experiments or simulations of protein folding.

BP 8.27 Mon 17:30 Poster B2

Inhibition of HIV-1 protease: the rigidity perspective — •Jack Heal[1], Emilio Jimenez-Roldan[2,3], Stephen Wells[2], Robert Freedman[3], and Rudolph Römer[2] — [1]MOAC Doctoral Training Center, University of Warwick, Coventry, UK, CV4 7AL — [2]Department of Physics, University of Warwick, Coventry, UK, CV4 7AL — [3]Department of Life Sciences, University of Warwick, Coventry, UK, CV4 7AL

HIV-1 protease is a key drug target due to its role in the life-cycle of the HIV-1 virus. There are more than 200 high resolution ($\leq$ 2 Å) X-ray crystal structures of the enzyme in complex with a variety of ligands. We have carried out a broad study of these structures using the rigidity analysis software FIRST. This approach allows us to make inferences about the effect of ligand binding upon the rigidity of the protein. The protease inhibitors currently used as part of antiretroviral treatments can be split into two categories, which may offer an explanation for the efficacy of particular combination therapies.

BP 8.28 Mon 17:30 Poster B2

Distance Dependency And Minimum Amino Acid Alphabets for Decoy Scoring Potentials — •Kay Hamacher — TU Darmstadt

Protein scoring potentials are a valuable tool in molecular biophysics to assess the quality of, e.g., a protein structure. Among those several knowledge-based potentials were developed in the past. However, continuous distance information have not been suggested yet. Here, we propose to close this methodological gap. This becomes possible as the parametrization problem can be formulated as a linear program, for which even large-dimensional instances can be solved efficiently. This allowed us to extended the study into assessing the usability of reduced amino acid alphabets.

[1] S. Pape, F. Hoffgaard, M. Dür, K. Hamacher, "Distance Dependency And Minimum Amino Acid Alphabets for Decoy Scoring Potentials", J. Comp. Chem., 34: 10-20, 2013.

BP 8.29 Mon 17:30 Poster B2

Non-Equilibrium MD simulations of intramolecular signaling in allosteric proteins — •Sebastian Waltz — Biomolecular Dynamics Physik Institut Uni-Freiburg

The interaction of a protein with another protein or ligand causes local energetic and or conformational changes of the protein around the binding side. This structural changes may propagate through the protein and produce functional changes at the distant side. This process is often referred to as allostery. There is an ongoing discussion about the signaling pathway and on the timescale on which the information travels along the protein. To resolve this open question, we perform intensive Non-equilibrium molecular dynamic simulations of a photoinduced conformational change and intramolecular signaling, that allow us to observe the functioning of the protein in real time. The goal is to directly prove the existence of dynamically driven pathways of intramolecular signaling.

BP 8.30 Mon 17:30 Poster B2

Pitfalls and artifacts in two-focus fluorescence fluctuation spectroscopy — •Andreas Veres and Matthias Weiss — Experimental Physics I, University of Bayreuth, Germany

Fluorescence fluctuation spectroscopy is a powerful technique to quantify intracellular transport on the almost single-molecule scale. Going beyond a single observation volume, temporally cross-correlating the fluorescence from two separated foci can be exploited to obtain large-scale transport coefficients, and to detect transport barriers or directed flow. Using mean-field theory and simulations in combination with experiments on a laser scanning microscope (LSM), we have investigated which artifacts and pitfalls may hamper this promising approach. We find that the unavoidable bleaching of fluorophores only has a minor influence on the results, whereas the typically poor statistics in commercial LSMs severely limits the applicability of the approach to in vitro systems.