BP 7: Posters: Proteins

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

BP 7.1   Mon 17:30   Poster A

Conformational energy hierarchy of benchmark polyalanine based peptides with secondary structure — ●Sucismita Chutia, Mariana Rossi, Volker Blum, and Matthias Scheffler — Fritz-Haber Institute, Berlin, Germany

An important challenge for the theoretical study of peptides and proteins is a faithful representation of the most stable conformations and their energy hierarchy. We here address the accuracy of a first-principles based conformational search approach for two polyalanine-based peptides that are well studied in vacuum experiments and can thus be considered "benchmark cases". We use a force-field based pre-screening of the astronomically large number of possible conformers, followed by thousands of post-relaxations using density functional theory (PBE) with corrections for van der Waals terms [1]. This approach yields good agreement with experiment for the polyalanine based peptide $Ac\text{-}Ala_5\text{-}LysH^+$ [2]. However, in the case of the equally well studied peptide $Ac\text{-}Phe\text{-}Ala_5\text{-}LysH^+$ [3], the experimentally observed structures at low temperature are not simply the lowest (potential) energy ones. By varying the density functional, we show that its accuracy could partially account for the discrepancy, but in addition, much better agreement with experiment would result by including room-temperature vibrational free energy contributions. We suggest that the predominance of the experimental conformers is affected by selection/freezing at room temperature. [1] A.Tkatchenko and M.Scheffler, PRL **102**, 073005 (2009). [2] M. Rossi *et al.*, J. Phys. Chem. Lett. **1**, 3465 (2010). [3] J.A. Stearns *et al.*, PCCP **11**, 125 (2009).

BP 7.2   Mon 17:30   Poster A

Characterization and Application of the redox-sensitive GFP-mutant roGFP — ●Sebastien Peter[1], Sebastian Wierer[3], Kirstin Elgass[4], Stefan Bieker[1], Alfred Meixner[2], Ulrike Zentgraf[1], and Frank Schleifenbaum[1] — [1]Zentrum für Molekularbiologie der Pflanzen, Universität Tübingen, Deutschland — [2]Institut für physikalische und theoretische Chemie, Universität Tübingen, Deutschland — [3]Protein Crystallography and Molecular Bioinformatics, Universität Konstanz, Deutschland — [4]Biochemistry Department, La Trobe University, Bundoora, Australia

For the quantitative analysis of molecular processes in living (plant) cells new combinatorial approaches in optical and spectroscopic technologies are required. The use of green fluorescent protein (GFP) and its variants has revolutionized the in vivo analysis of cell biological processes. More recently, fluorescent proteins have been designed and adapted for targeted sensing of cellular metabolites. Recent progress has been made in generating a redox- sensitive mutant of GFP (roGFP). Here, we characterize the optical properties of roGFP in dependence on the environmental redox state including a comprehensive comparison of different spectral analysis approaches in vitro. Furthermore, we demonstrate several applications of roGFP in living plants such as long-term redox potential readout in plant cells.

BP 7.3   Mon 17:30   Poster A

Simulating the infrared spectra of solvated molecules — ●Jonathan Brox, Sebastian Waltz, Maja Kobus, and Gerhard Stock — Biomolecular Dynamics, Physikalisches Institut, Universität Freiburg, Hermann-Herder-Str. 3, 79104 Freiburg

Advances in time-dependent two dimensional infrared spectroscopy (IR) give the possibility to resolve structural dynamics peptides and proteins in real time. In particular, the spectrum of the amide I mode is a sensitive probe for conformational dynamics. To model IR spectra, we need to calculate the instantaneous vibrational frequency. We simulate small peptides in water to estimate the intra- and intermolecular contributions to the frequency shift. Established models describe the influence of the solvent during the simulation to the amide I band in different ways. In this talk, we will compare first results from a force-field based ansatz by D. Oxtoby [1] with an ab initio based method [2] and an empirical map [3].
[1] D. Oxtoby, Annu. Rev. Phys. Chem. **32**, 77 (1981)
[2] R. Gorbunov, D. Kosov and G. Stock, J.Chem. Phys. 2005, **122**, 224904
[3] L. Wang, C. Middleton, M. Zanni and J. Skinner, J. Phys. Chem. B 2011, **115**, 3713

BP 7.4   Mon 17:30   Poster A

Macromolecular unfolding properties in presence of compatible solutes — ●Jens Smiatek[1], Hans-Joachim Galla[2], and Andreas Heuer[1] — [1]Institut für Physikalische Chemie, WWU Münster, D-48149 Münster, Germany — [2]Institut für Biochemie, WWU Münster, D-48149 Münster, Germany

We present Molecular Dynamics simulations of Chymotrypsin inhibitor II and PEO in presence of compatible solutes. Our results indicate that the native compact state of the studied macromolecules is stabilized in presence of hydroxyectoine. We are able to explain the corresponding mechanism by a variation of the solvent properties for higher hydroxyectoine concentrations. Our results are validated by detailed free energy calculations.

BP 7.5   Mon 17:30   Poster A

Dynamic disorder in enzyme catalyzed reactions: a general phenomenon? — Tatyana Terentyeva[1], Hans Engelkamp[2], Alan E. Rowan[2], Tamiki Komatsuzaki[3], Johan Hofkens[1], Chun-Biu Li[3], and ●Kerstin Blank[2] — [1]Katholieke Universiteit Leuven, Department of Chemistry, Leuven, Belgium — [2]Radboud University Nijmegen, Institute for Molecules and Materials, Nijmegen, The Netherlands — [3]Hokkaido University, Research Institute for Electronic Science, Sapporo, Japan

Single molecule fluorescence experiments allow the recording of the sequence of individual enzymatic turnover reactions. Experiments with different enzymes have shown that the waiting times between turnovers follow a stretched exponential distribution interpreted as dynamic disorder. Although easily explained with the existence of several enzyme conformations with different activity the question remains if dynamic disorder is a general property of enzymes. Studying the enzyme chymotrypsin we observe deviations from a stretched exponential distribution. Moreover, we see obvious differences in the shape of the waiting time distributions depending on the data analysis method used. Comparing the performance of the most widely employed binning and thresholding approach with change point analysis we observe that the underlying on- and off-histograms are not necessarily extracted from the "signal" buried in noise. When using the more accurate change point analysis for data of chymotrypsin no characteristics of dynamic disorder can be found. In light of these new results, dynamic disorder might not be a general characteristic of enzymatic reactions.

BP 7.6   Mon 17:30   Poster A

Molecular Dynamics Simulations of Hydrated Proteins: Possible Origins of a Logarithmic Protein Relaxation. — ●Kerstin Kämpf and Michael Vogel — TU Darmstadt, Institut für Festkörperphysik, 64289 Darmstadt

Biological function is the consequence of protein fluctuations in a complex energy landscape. An unresolved puzzle of protein dynamics is the origin of a strongly nonexponential relaxation observed over several orders of magnitude in time.

In order to elucidate this phenomenon, we perform molecular dynamics simulations of hydrated elastin and myoglobin. It is observed that the orientational and translational correlation functions of the protein backbone are well described by a power law [1] or a logarithmic decay [2]. Assuming a heterogeneous origin of the power-law decay, we analyze the temperature dependent mean relaxation rates. An Arrhenius behavior with an activation energy $E_a \approx 0.25$ eV is obtained, corresponding to the energy necessary to break a hydrogen bond. Fitting to a logarithmic decay, we tested whether the predictions of the mode-coupling theory are fulfilled. We investigate further how far the dynamics of hydrated proteins resemble that of other complex systems.

Finally, we calculate multi-time correlation functions to determine the relevance of homogeneous and heterogeneous contribution to the strongly nonexponential decay. This analysis allows to characterize the complex energy landscape and thus to shed light on the nature of the microscopic processes underlying protein function.
[1] Iben et al. PRL 62, 1916. [2] Lagi et al, PRL, 103, 108102.

BP 7.7   Mon 17:30   Poster A

How cations change peptide conformation: First principles simulations and infrared spectroscopy — ●Carsten Baldauf[1], Kevin Pagel[1], Volker Blum[1], Stephan Warnke[1], Gert von

Helden[1], Beate Koksch[2], Gerard Meijer[1], and Matthias Scheffler[1] — [1]Fritz-Haber-Institut der MPG, Berlin — [2]Institut für Chemie und Biochemie, FU Berlin

Turns are the hinges arranging periodic secondary structure elements (helices and strands) to form compact protein tertiary folds. Li^{+} alters protein backbone conformation. We investigate this effect on structure and dynamics of turns Ac-Ala-{Ala,Asp}-Pro-Ala-NMe by theoretical conformational analyses and experimental vibrational spectroscopy. As standard force fields apparently lack accuracy for ion-peptide interactions, we demonstrate a trustworthy description of the potential-energy surface of these systems by van der Waals corrected density-functional theory (PBE+vdW) and compare to gas-phase infrared spectroscopy, both approaches in the exact-same clean-room environment. We predict canonical turn conformations for the peptides alone. Li^{+} and Na^{+} adsorb to C=O groups, induce unusual backbone conformations, and prevent H bond formation. By including free-energy contributions, essential for consistent theory-experiment comparison, we show that multiple conformers coexist at room temperature. First-principles molecular dynamics simulations lead to theoretical spectra (including anharmonic effects) which indicate low-energy conformers do not equally contribute to the experimental spectra. They also give insights into backbone motion patterns (peptide bond crankshaft rotation).

BP 7.8 Mon 17:30 Poster A

Chloroplast fluorescence excitation and emission spectroscopy in live plant cells — ●Sebastien Peter[1], Martina Zell[5], Christian Blum[3], Kirstin Elgass[4], Veronica Maurino[5], Alfred Meixner[2], Vinod Subramaniam[3], and Frank Schleifenbaum[1] — [1]Zentrum für Molekularbiologie der Pflanzen, Universität Tübingen, Deutschland — [2]Institut für physikalische und theoretische Chemie, Universität Tübingen, Deutschland — [3]Biophysical Engineering, University of Twente, Enschede, The Netherlands — [4]Biochemistry Department, La Trobe University, Bundoora, Australia — [5]Botanisches Institut, Universität zu Köln, Deutschland

Statistical analysis of chloroplast fluorescence spectra recorded at room temperature enables for drawing conclusions about the relative PSI/PSII ratio in wild type and carbon deficient plant cells. Leaf cells exhibit fluorescence from chloroplasts whose spectra show two bands assigned to the photosystems. Changes in a plant's environmental conditions are reflected by an altered efficiency of photosynthesis. Fluorescence excitation spectra of plants grown under different conditions show three peaks assigned to different carotenoids. The spectra not only differ in the intensity ratios between different pigments but also in the broadth of their distributions revealing a higher adaptation flexibility of wild-type plants. Therefore, fluorescence excitation and emission spectroscopy at room temperature enables for live read-out of the photosynthesis adaption to external conditions without generating artifacts from extensive sample preparation and low temperatures.

BP 7.9 Mon 17:30 Poster A

Ab initio Molecular Dynamics & NMR Spectra of Phycocyanobilin in the α-C-Phycocyanin binding pocket — ●Hossam Elgabarty and Daniel Sebastiani — Freie Universität Berlin Fachbereich Physik Arnimallee 14 14195 Berlin

Biliproteins are ubiquitous photoreceptors. On exposure to red light the bound bilin chromophore exhibits a very quick photoisomerization within a few picoseconds [1]. Interactions between the bilin and its binding pocket play a crucial role in this process. We have performed ab-initio QM/MM molecular dynamics simulations of phycocyanobilin bound to the C-subunit of α-C-phycocyanin. Our results provide insight into the nature of the local interactions around the chromophore. Calculations of ^{14}N and ^{1}H NMR shifts are in good agreement with experimental spectra and demonstrate that the chromophore is stably protonated in acccord with experimental findings [2]. Our results pave the way to further investigation of the photocycle by exploiting the sensitivity of NMR spectra to local environment [3].

1 Ulijasz, A. T., Vierstra, R. D. Curr. Opin. Plant Biol., 14, 498-506. (**2011**)

2 Hahn, J., Kühne, R., Schmieder, P. ChemBioChem, 8, 2249-55. (**2007**)

3 Elgabarty, H., Röben, M., Schmieder, P., Sebastiani, D. (Submitted)

BP 7.10 Mon 17:30 Poster A

Many-Body study of the excited-state properties of the Retinal Protonated Schiff Base of Rhodopsin — ●Adriano Mosca Conte[1], Leonardo Guidoni[2], Daniele Varsano[3], and Olivia Pulci[1] — [1]MIFP, NAST, ETSF,CNR INFM-SMC, University of Rome Tor Vergata, Via della Ricerca Scientifica 1, Roma, Italy — [2]University of L'Aquila, Dipartimento di Chimica, Ingegneria Chimica e Materiali, Via Campo di Pile, 67100, L'Aquila, Italy — [3]University of Rome "La Sapienza" , P.le Aldo Moro 2, Rome, Italy

The first step of the mechanism of vision in living creatures is the photo-isomerization of the rhodopsin chromophore: the protonated Schiff base of the 11-cis retinal. We investigate the optical properties of the tZt-penta-3,5-dieniminium cation, a simplified model for the retinal, along the isomerization pathway by ab-initio calculations based on Many-Body Perturbation Theory (GW method and the Bethe-Salpeter equation), and by TDDFT. Our excitation energies are qualitatively in agreement with previous Quantum Monte Carlo and Post-Hartree Fock calculations. We then investigate the effect of the protein environment on the optical absorption spectra of the 11-cis retinal, in gas phase and in the rhodopsin. We follow a Quantum-Mechanics/Molecular-Mechanics scheme in which the retinal is treated by quantum Many-Body methods (DFT+GW+BSE), while the surrounding atoms of the protein are treated according to a classical model. Our results show that the effect of the rhodopsin on the retinal produces a geometrical distorsion of the retinal and a blueshift on the absorption spectrum in good agreement with the experiments.

BP 7.11 Mon 17:30 Poster A

A method to construct the free energy landscape of peptide aggregation from molecular dynamics simulations. — ●Laura Riccardi, Phuong H. Nguyen, and Gerhard Stock — Biomolecular Dynamics, Institute of Physics, Albert Ludwigs University, 79104 Freiburg, Germany

A broad range of diseases are associated with the conversion of polypeptide chains from their normally soluble form to insoluble fibrillar aggregates. One of the most studied pathogenic peptides is the Alzheimer β-amyloid peptide, and its fragment $A\beta_{16-22}$ appears to be a perfect model system as it is among the shortest fragments which are able to form fibrils [1]. We propose a new method to identify and characterize the different conformational states occurring during the aggregation process. This method is general as no *a priori* knowledge of the dynamics of the process or the structure of the encounter complex is required. In the different steps, intramolecular and intermolecular interactions are considered as well as the degeneracy of the multi-molecule system. The obtained states are used to construct a network which reflects the free energy landscape of the process and helps to identify the aggregation pathways.

[1] P.H. Nguyen et al, Monomer adds to preformed structured oligomers of $A\beta$-peptides by a two-stage dock-lock mechanism. PNAS 104, 111 (2007)

BP 7.12 Mon 17:30 Poster A

Ab initio **conformation trends across 20 amino acids, dipeptides, and their interaction with divalent ions** — ●Matti Ropo, Carsten Baldauf, Volker Blum, and Matthias Scheffler — Fritz-Haber-Institut der Max-Planck-Gesellschaft, Berlin, Germany

Ion-protein interactions are of tremendous importance in cellular signalling of all organisms. For instance, the binding properties of Ca^{2+} can be mimicked by heavy metals like Pb, thus disturbing Ca-dependent functions[1]. We have constructed an exhaustive, first-principles based conformational (*in vacuo*) database of the 20 proteinogenic amino acids, their dipeptides, and of their interactions with the divalent cations of Ca, Sr, Ba, Cd, Pb, and Hg. The database was established using all-electron density functional theory with the van der Waals-corrected PBE functional.[2] We here use it to discuss trends of biological interest, for example: (i) a uniform binding order of ions relative to Ca^{2+}—Sr^{2+} and Ba^{2+} bind weaker, Pb^{2+} binds similar, Cd^{2+} and Hg^{2+} stronger. (ii) Dipeptides bind cations stronger than amino acids alone. (iii) Interestingly, Ca^{2+} binds strongest to Arg and Tyr, not to Asp or Glu (assuming the neutral protonation state for the amino acids). (iv) We evaluate backbone conformations by means of Ramachandran plots and atomic distribution function and compare these data sets to experimental structural data from the RCSB protein data bank. Finally, we address the impact of density functionals beyond the generalized gradient approximation. [1] H.A. Godwin, Curr. Opin. Chem. Biol. **5**, 223 (2001); [2] A. Tkatchenko and M. Scheffler,

PRL **102**, 73005 (2009).

BP 7.13 Mon 17:30 Poster A

Lactoferrin: dynamics of a flexible protein in solution investigated by neutron scattering — •Clemens Sill[1], Ralf Biehl[1], Bernd Hoffmann[2], and Dieter Richter[1] — [1]JCNS-1 & ICS-1, Forschungszentrum Jülich, 52425 Jülich, Germany — [2]ICS-7, Forschungszentrum Jülich, 52425 Jülich, Germany

The understanding of the functionality of proteins started with a rigid model, namely the Lock and Key analogy, in 1894. Meanwhile, a more dynamic and flexible picture of these macromolecules has evolved to explain protein function like catalyzing biochemical reactions, transport, regulation, storage or defensive tasks. The importance of thermodynamically driven, internal motions for the functioning of proteins is subject of ongoing research.

We will present recent investigations of protein dynamics on Lactoferrin, a protein with antimicrobial activity which is part of the innate immune system. It consists of two binding sites, each is capable of binding and releasing one iron ion. The crystallographic structures show that the binding sites have open and closed conformations, assumedly depending on the presence of iron. We are analyzing the internal dynamics of different binding states to elucidate the binding mechanism with neutron scattering. Our unique method includes large scale structural characterization with small angle neutron scattering and the observation of internal motions of subdomains with neutron spin echo spectroscopy on nanosecond scale. This combination provides the opportunity to investigate the link between binding mechanism, internal dynamics and conformational change.

BP 7.14 Mon 17:30 Poster A

The class IIa Water soluble chlorophyll binding protein (WSCP) from cauliflower can be described by an electronically strongly coupled dimer bound to two different protein configurations — •Franz-Josef Schmitt[1], Jörg Pieper[2], Christoph Theiss[1], Inga Trostmann[3], Harald Paulsen[3], Thomas Renger[4], Hans Joachim Eichler[1], Thomas Friedrich[1], and Gernot Renger[1] — [1]Berlin Institute of Technology, Germany — [2]University of Tartu, Estonia — [3]Johannes Gutenberg University Mainz, Germany — [4]Johannes Keppler University Linz, Austria

Spectroscopic studies on pigment-pigment and pigment-protein interactions of chlorophyll (Chl) a and b bound to the recombinant protein of class II a WSCP from cauliflower were performed with absorption and fluorescence spectroscopy in the time domain of fs and ps, respectively, providing evidence for spectral inhomogeneity in these samples even if the WSCP contains only homodimers. In class II a WSCP two Chls form a strongly excitionally coupled open sandwich dimer within the tetrameric protein matrix. A modulation of the electronic states of the coupled Chl dimer by the protein environment with a typical time constant of 100 ps at 10 K is inferred to be responsible for a fast and strongly temperature dependent fluorescence component. This idea is in line with refined theoretical models and results of complementary studies of hole burning and fluorescence line narrowing spectroscopy. We show that the time resolved fluorescence spectra can be simulated with rate equation models based on results obtained with recent FLN and hole burning studies.

BP 7.15 Mon 17:30 Poster A

Determination of the hydrodynamic radius of GFP-tagRFP FRET-Constructs with Fluorescence Correlation Spectroscopy — •Patrick Hätti[1], Franz-Josef Schmitt[2], Cornelia Junghans[2], Marco Vitali[2], and Thomas Friedrich[2] — [1]Institute of Optics and Atomic Physics, Berlin Institute of Technology, Germany — [2]Max Volmer Laboratory for Biophysical Chemistry, Berlin Institute of Technology, Germany

Fluorescence correlation spectroscopy (FCS) is suitable to determine the hydrodynamic radius of single molecules and protein chromophors by taking the $G(\tau)$ autocorrelation function and calculating the diffusion time. FCS and fluorescence lifetime measurements were done simultaneously with a novel Fluorescence Lifetime Imaging Microscopy setup (FLIM) with an integrated Single-Photon-Avalanche-Diode (SPAD). We determined the hydrodynamic radius of Green Fluorescent Protein to 3.2 nm. A FRET-construct consisting of the GFP-tagRFP fusion protein was observed with a much larger hydrodynamic radius of 12.6 nm, which might be explained by a more complex geometrical structure of the molecule that has more degrees of freedom. GFP and tagRFP are linked via a 5 amino acid-long linker that connects the two single, barrel-shaped fluorescent proteins. In addition to

FCS, the setup allows the determination of the fluorescence lifetimes and therefore the calculation of the center-to-center distance of the molecular transition dipoles according to the theory of Förster Resonance Energy Transfer, which is compared with the hydrodynamic radius.

BP 7.16 Mon 17:30 Poster A

Characterization of novel bimolecular fluorescence complementation (BiFC) protein complexes by single-molecule spectroscopy — •Sven zur Oven-Krockhaus[1], Sebastien Peter[1], Alfred Meixner[2], Klaus Harter[1], and Frank Schleifenbaum[1] — [1]Zentrum für Molekularbiologie der Pflanzen, Tübingen, Deutschland — [2]Institut für physikalische und theoretische Chemie, Tübingen, Deutschland

The identification and characterization of protein-protein interaction networks in living organisms is of major importance in current proteome sciences. Bimolecular fluorescence complementation (BiFC) constitutes an innovative method to visualize interaction partners in living cells. As this technique utilizes molecular markers, a competent knowledge of their photophysical properties is essential. In the case of multicolor BiFC, two nearby fragments of different GFP mutants can spontaneously recombine to a functional fluorescent protein complex. Even though they only differ in few amino acids, differently composed complexes show a significant diversity in their spectroscopic properties. As many photophysical features are concealed in bulk measurements, a single molecule approach has been employed to characterize model systems of these BiFC complexes. Several hundred single molecule spectra and fluorescence intensity time traces were accumulated in order to identify the spectroscopically most relevant amino acids in the protein shell structure - uniquely revealing their influence on the shells' mechanical flexibility.

BP 7.17 Mon 17:30 Poster A

Calculation of the CD spectrum of a peptide from its conformational phase space — •Zlatko Brkljača[1], Karmen Čondić-Jurkić[1], David M. Smith[2], and Ana-Sunčana Smith[1] — [1]Institut für Theoretische Physik, Universität Erlangen-Nürnberg, Erlangen, Germany — [2]Computer Chemie Centrum, Universität Erlangen-Nürnberg, Erlangen, Germany

Met-enkephalin (Tyr-Gly-Gly-Phe-Met) and its unnatural analogue Ada-enkephalin are opioid peptides which act as inhibitors of tumor-cells in a receptor-mediated fashion. We have investigated the structural preferences of these peptides in 2,2,2-trifluoroethanol in an attempt to calculate their respective CD spectra. To this end, we have characterized the conformational preferences of the zwitterionic and neutral forms of Met-enkephalin and of both the R- and the S-epimers of Ada-enkephalin, as obtained by replica exchange molecular dynamics. The CD spectrum for each peptide was subsequently obtained with a procedure of successive averaging, which accounts for the sidechains and the backbone variations of the peptides and the effect of the solvent on the CD spectra. To make a proper comparison with the experiment, we have produced composite spectra that account for the appropriate contributions of the zwitterionic and neutral forms of the peptides as well as the expected epimeric ratio. Such a procedure results in theoretically obtained CD spectra that successfully reproduce the most important features of the experimentally measured spectra. Consequently, the link between the CD spectra and the conformational phase space of flexible peptides can be established for the first time.

BP 7.18 Mon 17:30 Poster A

Combined time-resolved and integrated analysis of FRET efficiency in genetically expressed GFP-tagRFP fusion proteins — •Jörn Weissenborn[1], Franz-Josef Schmitt[2], Patrick Hätti[1], Cornelia Junghans[2], Oliver Schöps[1], Ulrike Woggon[1], and Thomas Friedrich[2] — [1]Institute for Optics and Atomic Physics, Berlin Institute of Technology, Germany — [2]Max Volmer Laboratory for Biophysical Chemistry, Berlin Institute of Technology, Germany

Förster resonance energy transfer (FRET) was investigated in constructs consisting of GFP-tagRFP fusion proteins with varying distance between donor and acceptor. In the short and long construct, GFP and tagRFP are linked via a 5 and 13 amino acid-long linker, respectively, that connects the two single, barrel-shaped fluorescence proteins. Interestingly, a strong donor quenching of the short-linker FRET construct does not lead to a concomitant rise of the acceptor fluorescence (RFP) with the same amplitude. An accurate analysis of 2-dimensional photoluminescence excitation spectroscopy (PLE) and time-and wavelength resolved fluorescence decay showed congruent re-

sults. The data analysis reveals that only 50 % of the GFP molecules are coupled to tagRFP via excitation energy transfer (EET). The efficiency of the EET in the coupled GFP-tagRFP pairs calculates to about 65 %. According to our experiments and the FRET theory, the long-linker construct should show virtually no EET. The overall transfer efficiency (coupled and uncoupled species) is calculated to 30 % and < 1 % in the short- and long-linker FRET construct, respectively.

BP 7.19   Mon 17:30   Poster A

Ribonuclease A: A Model System to Study Structure and Dynamics of Disordered Proteins — •Jennifer Fischer[1], Ralf Biehl[1], Bernd Hoffmann[2], and Dieter Richter[1] — [1]Forschungszentrum Jülich, ICS-1, Jülich, Germany — [2]Forschungszentrum Jülich, ICS-7, Jülich, Germany

Up to know structure and dynamics are believed to play the key role in protein function. Now it is evident that roughly 30% of eukaryotic proteins are partially or even completely unfolded [1]. Nevertheless, intrinsically unfolded proteins are functional and involved in several biological processes. To get further insight into disordered structures and their dynamics, we use Ribonuclease A (RNase A) as a model system, as it is a well known protein denaturing reversibly upon heating. Additionally, by varying the buffer conditions such as pH values and by reducing the disulfide bonds, several states can be prepared. A detailed study of the structure and dynamics using Small Angle Neutron and X-ray Scattering (SANS, SAXS) as well as Neutron Spin Echo Spechtroscopy (NSE) and Circular Dichroism Spectroscopy is presented. The combination of these techniques allows us to observe large-scale internal dynamics of subdomains or of unfolded protein strands that operate on the same length scale as rotational diffusion. However, the timescale can be different and depends on the protein structure and internal interactions. [1] A. L. Fink, Current Opinion in Structural Biology 2005, 15:35-41

BP 7.20   Mon 17:30   Poster A

Probing peptide structure prototypes with first-principles replica exchange: Ac-Ala$_{19}$-LysH$^+$ vs. Ac-LysH$^+$-Ala$_{19}$ — •Franziska Schubert, Mariana Rossi, Carsten Baldauf, Volker Blum, and Matthias Scheffler — Fritz-Haber-Institut der MPG, D-14195 Berlin

Predicting the structure of peptides requires a method with high accuracy for "weak" interactions. We here focus on the predominant structure types of two alanine-based peptides under "clean-room" conditions in the gas phase from first principles and in comparison to experimental IR spectroscopy [1]: Ac-Ala$_{19}$-LysH$^+$, which is α-helical [2,3], in contrast to Ac-LysH$^+$-Ala$_{19}$, where mostly globular monomers and a small amount of helical dimers and helices with non-standard protonation sites are expected [3]. Despite supposedly very different conformers, Ac-LysH$^+$-Ala$_{19}$ and Ac-Ala$_{19}$-LysH$^+$ yield very similar experimental IR spectra in the $\approx$1000-2000 cm^{-1} wavenumber range. We suggest plausible candidates for all likely structure prototypes generated by a two-step structure search: On top of force-field based replica exchange molecular dynamics (REMD) scans we follow up with further REMD scans based on density functional theory with the van der Waals corrected [4] PBE functional. Helix-turn-helix motifs emerge as the most likely candidates and explain a subtle peak shift in experiment. [1] IRMPD experiments: G. von Helden, P. Kupser, K. Pagel, F. Filsinger, G. Meijer, Department of Molecular Physics, Fritz-Haber-Institut; [2] M. Rossi *et al.*, JPCL **1**, 3465 (2010); [3] M. Jarrold, PCCP **9**, 1659 (2007); [4] A. Tkatchenko, M. Scheffler, PRL **102**, 073005 (2009).

BP 7.21   Mon 17:30   Poster A

Solvent induced isomerization in phycocyanobilin — •Tobias Watermann, Hossam Elgabarty, and Daniel Sebastiani — Freie Universität Berlin, Fachbereich Physik, Arnimallee 14, 14195 Berlin

Phytochromes belong to the family of light detecting proteins, that are responsible for the reaction of biological systems to light. Their central functional part is a chromophore, which isomerizes upon excitation and initializes the signaling process of the protein. Recent NMR experiments [1] on the isolated chromophore phycocyanobilin show differing spectroscopic properties for different solvents. We investigate the underlying conformational space by means of ab-initio molecular dynamics and free energy calculations as well as ab-initio spectroscopy [2]. It turns out that it is of crucial importance to include the explicit solvent and its interaction with the chromophore. In our ab-initio molecular dynamics simulations, we observe specific preferences for certain conformations as a function of the polarity of the solvent. These computational results are confirmed by comparing ab-

initio NMR chemical shifts in the different situations to corresponding experiments. This solvent dependent effect can be traced back to a change in the equilibrium between intra- and intermolecular hydrogen bonds of the chromophore and the solvent.

1 M. Röben, P. Schmieder, Magn. Reson. Chem., 49, 543-548 (**2011**)

2 T. Watermann, H. Elgabarty, M. Röben, P. Schmieder, D. Sebastiani (Submitted)

BP 7.22   Mon 17:30   Poster A

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

Tip-enhanced Raman spectroscopy (TERS) combines high spatial resolution of atomic force microscopy (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 30 nm.

AFM allows imaging, measuring (e.g.: single-molecule force spectroscopy), and manipulating matter at the nanoscale. The information is gathered by "feeling" the surface with a mechanical probe.

Raman spectroscopy provides information about the molecular structure of proteins. In order to detect a monolayer of molecules we use surface-enhanced Raman spectroscopy (SERS). The SERS signal is enhanced in the vicinity of (usually) silver- or gold-coated surfaces (up to a factor of $10^9 - 10^{12}$ compared to conventional Raman).

Up to now, this technique is mainly applied to surfaces modified with inorganic samples. However, TERS is a promising tool to investigate membrane proteins since single molecules could be studied by Raman spectroscopy under biological conditions.

Here, we introduce the experimental setup and discuss the application of TERS to the investigation of membrane proteins.

BP 7.23   Mon 17:30   Poster A

Investigation of the PhoB-Interaction with the DNA - minor groove by Single Molecule Force Spectroscopy — •Adeline Bieker[1], Volker Walhorn[1], Gesa Niemann[2], Markus Ritzefeld[2], Norbert Sewald[2], and Dario Anselmetti[1] — [1]Experimental Biophysics and Applied Nanoscience, University of Bielefeld, Germany — [2]Organic and Bioorganic Chemistry, University of Bielefeld, Germany

Interactions between proteins and DNA are essential for the regulation of cellular processes in all living organisms. In this context, it is of special interest to investigate and quantify the sequence-specific molecular recognition between transcription factors and their cognate DNA sequences [1].

We investigated point mutated proteins originating from the DNA-binding domain (DBD) of the Escherichia coli transcription factor PhoB. By means of AFM-based Single Molecule Force Spectroscopy (SMFS) we acquired binding forces and molecular elasticities to elucidate the complex stability. Based on the Bell-Evans-Modell [2] we estimated the thermal dissociation rate constants (k_{off}) and the molecular interaction length (x_β), that allowed a structure related interpretation of the physical binding mechanisms involved.
[1] Small. 2009 Apr;5(4):484-495.
[2] Biophys. J. 1997;72:1541-1555.

BP 7.24   Mon 17:30   Poster A

A Coarse-Grained Model for Protein Backbone Dynamics — Andreas Wagenmann and •Tihamer Geyer — Zentrum f. Bioinformatik, Universität des Saarlandes, Saarbrücken

When one wants to simulate the folding of proteins or the dynamics of intrinsically disordered proteins, atomistic simulations very soon become prohibitively expensive. This is even more so when multiple proteins are considered as for example in the case of amyloid formation. For these scenarios coarse-grained models are required. Here we present a newly developed hierarchic coarse-grained model which builds upon Langevin Dynamics. Using this very efficient solvent-free simulation technique allows for more freedom in the modeling than a united-atom-approach with its still spherical super-atoms. Here we show how we base the model of the protein backbone on non-spherical building blocks with off-center bonds. By construction, the allowed regions in the Ramachandran angle space are reproduced. Non-local steric interactions, electrostatics, and hydrogen bonds form a second layer and modify the secondary structure propensities according to the

residue types. We also demonstrate that poly-peptides form alpha-helical or beta-strand structures according to their amino-acid composition even when we start from random initial configurations. This model can be used to efficiently simulate the folding and association of unfolded proteins like Amyloid-β or α-synuclein.

BP 7.25   Mon 17:30   Poster A

Using Dynamic Graphs to Quantitatively Visualize Agglomeration in Spatial Simulations — •Tihamer Geyer[1], Florian Lauck[2], and Volkhard Helms[1] — [1]Zentrum für Bioinformatik, Universität des Saarlandes, Saarbrücken — [2]Dept. of Bioengineering and Therapeutic Sciences, UCSF, San Francisco, USA

The usual approaches to analyze many-particle simulations of association processes either focus on time-averaged measures for the degree of binding like radial distribution functions or cluster sizes, or movies are generated which in principle provide all the details but in an only qualitative way. Here we show how dynamic graphs can be used to visualize quantitatively the time dependent events of complex formation and breaking. For this, a simple distance criterion is used to set up a time dependent graph from the snapshots of the spatial simulation [1]. Some examples highlight how even simple graph measures like the degree distribution or the clustering coefficient can be used to follow the dynamics, to unambiguously identify complexes in a sea of monomers and partially assembled fragments, or to quantify how regular or amorphous an aggregate is [2]. In a further step the spatial simulation and the dynamic graph will be combined such that the simulation can make use of the connectivity encoded in the graph by, e.g., defining temporary pseudo-particles or different diffusion coefficients based on how many neighbors are actually bound.

[1] F. Lauck, V. Helms, T. Geyer, *J. Chem. Theor. Comput.* **5** (2009) 641

[2] T. Geyer, *BMC Biophys.* **4** (2011) 7

BP 7.26   Mon 17:30   Poster A

Investigations of the Dynamics of Protein Hydration Water, Water in an amorphous Ice Confinement and bulk Water, performed with molecular dynamics Simulations — •Felix Klameth and Michael Vogel — Institut für Festkörperphysik, TU Darmstadt, 64289 Darmstadt

The hydration water of proteins is essential for the biological function of proteins. For Myoglobin, large fluctuations of the protein structure enable oxygen diffusion to the protein heme-group. It was proposed, that water dynamics slave the protein motion [1], but till now the explicit mechanisms of protein water coupling are not understood. In order to clarify the protein-water interaction we study the dynamics of protein hydration water. We perform molecular dynamics simulations in a temperature range from 180 K up to 300 K. To unravel specific effects at the protein surface, we compare the results for the protein hydration water with that of bulk water and of water confined in amorphous ice. There are differences observed in the water-dynamics in this systems. The temperature dependence of the α-relaxation shows an Arrhenius-behaviour for the protein-hydration water, whereas a Vogel-Fulcher-Tammann-behaviour was observed for the bulk- and the confined water. Near both surfaces, protein and ice, the relaxation times of water are increased, compared to that of bulk. The mechanisms for this characteristics are not understood so far.

[1] Frauenfelder et al, PNAS 106 (2009)

BP 7.27   Mon 17:30   Poster A

The Impact of Salt and Pressure on the Interaction Potential of Proteins in Solution — •Johannes Möller[1], Martin A Schroer[1], Mirko Erlkamp[2], Sebastian Grobelny[2], Michael Paulus[1], Andre Steffen[1], Sebastian Tiemeyer[1], Florian J Wirkert[1], Metin Tolan[1], and Roland Winter[2] — [1]Fakultät Physik/DELTA, TU Dortmund, Otto-Hahn-Str. 4, 44227 Dortmund — [2]Physikalische Chemie, TU Dortmund, Otto-Hahn-Str. 6, 44227 Dortmund

The fabrication of crystals from protein solution has become the defining task in obtaining high resolution protein structures by X-ray diffraction. Here, the use of salt in the solution is commonly known to increase attractive interactions and therefore *salting out* the proteins. Nevertheless, the fabrication of high quality crystals is still a challenging task, due to the many different influences on the interactions in the protein solution, e.g. temperature, ionic strength, protein concentration, and pressure. We present the results of Small Angle X-ray Scattering experiments, which reveal the combined influence of hydrostatic pressure and ionic strength on the interaction potential

of dense protein solution. Here, a more precise knowledge about the interaction between proteins in solution can help to predetermine possible crystallization conditions, which is even more important when only a small amount of protein is available.

BP 7.28   Mon 17:30   Poster A

Aggregation of Human Antimicrobial Peptide Fragments at Interfaces — •Claudia Dannehl[1], Thomas Gutsmann[2], and Gerald Brezesinski[1] — [1]Max Planck Institute of Colloids and Interfaces, Science Park Golm, 14424 Potsdam — [2]Research Center Borstel, Center for Medicine and Biosience, 23845 Borstel

Antimicrobial peptides (AMPs) are short, amphiphilic proteins and part of the host immune defense. They protect organisms against bacteria, viruses and fungi simply by disrupting their membrane. In our work, we focus on two fragments of the human cathelicidin and lipid monolayers as model membranes to get insight into this peptide-lipid interaction. It was shown by XR and IRRAS, that both peptides adopt an alpha-helical conformation, when adsorbed to lipid monolayers, but differ in their way of action. Both peptides lead to a fluidization of a negatively charged DPPG monolayer, indicated by an increased transition pressure from a liquid-like to a liquid-condensed phase (seen by GIXD and IRRAS), but the increase in surface pressure and the change in the amide band upon adsorption is peptide specific. We assume that the stronger peptide-lipid interaction of one peptide is accompanied by a peptide aggregation at the interface, as studied by IRRAS on monolayers and CD spectroscopy with SDS in bulk (above the CMC). No changes in the spectra were recorded with IRRAS for zwitterionic lipids (DPPC, DOPC) and CD for the cationic CTAB , which means that the aggregation of the peptide is dominated by the charge density of the target.

BP 7.29   Mon 17:30   Poster A

CD-spectroscopy as a tool for characterizing protein-polymer complexes — •Sven Brandt[1], Krystin Krauel[1], Kay E. Gottschalk[2], Christiane A. Helm[3], and Stephan Block[1] — [1]ZIK HIKE - Zentrum für Innovationskompetenz Humorale Immunreaktionen bei kardiovaskulären Erkrankungen,, Fleischmannstr. 42-44, D-17487 Greifswald, Germany — [2]Institut für Experimentelle Physik, Universität Ulm, D-89069 Ulm — [3]Institut für Physik, Ernst-Moritz-Arndt Universität, Felix-Hausdorff-Str. 6, D-17487 Greifswald, Germany

Aggregates of platelet factor 4 (PF4), a highly positively charged protein that is stored in platelet alpha-granules, and natural or artificial polyanions are formed. Changes in the proteins secondary structure are monitored with circular dichroism (CD) spectroscopy, while the polyanion concentration is varied systematically. We observe pronounced structural changes of the PF4 during the interaction with highly charged polyanions. At a specific protein/monomer ratio the structural changes of the protein are most pronounced, suggesting that all proteins are incorporated into PF4-polyanion complexes. Only minor or no changes are found for weakly charged and neutral polymers. Interestingly, the most striking changes are observed for those PF4-polyanion complexes which are known to be immunogenic, such as aggregates with heparin, which can induce the life-threatening immune disorder called heparin-induced thrombocytopenia (HIT).

BP 7.30   Mon 17:30   Poster A

Probing the Transport of Ionic Liquids in Aqueous Solution through Nanopores — •Niraj Modi, Pratik Raj Singh, Kozhinjampara R. Mahendran, Robert Schulz, Mathias Winterhalter, and Ulrich Kleinekathöfer — School of Engineering and Science, Jacobs University Bremen, Campus Ring 1, 28759 Bremen, Germany

The temperature-dependent transport of the ionic liquid 1-butyl-3-methyl-imidazolium chloride (BMIM-Cl) in aqueous solution is studied theoretically and experimentally. Using molecular dynamics simulations and ion-conductance measurements, the transport is examined in bulk as well as through a biological nanopore, i.e., OmpF and its mutant D113A. This investigation is motivated by the observation that aqueous solutions of BMIM-Cl drastically reduce the translocation speed of DNA or antibiotics through nanopores in electrophysiological measurements. This makes BMIM-Cl an interesting alternative salt to improve the time resolution. In line with previous investigations of simple salts, the size of the ions and their orientation adds another important degree of freedom to the ion transport, thereby slowing down the transport through nanopores. An excellent agreement between theory and conductance measurements is obtained for wild-type

OmpF and a reasonable agreement for the mutant. Moreover, all-atom simulations allow an atomistic analysis revealing molecular details of the rate-limiting ion interactions with the channel[1].

[1] N. Modi et al., J. Phys. Chem. Lett. 2, 2331 (2011).

BP 7.31   Mon 17:30   Poster A

Computersimulation of protein adsorption on polyelectrolyte brushes — •Cemil Yigit[1] and Joachim Dzubiella[2] — [1]Helmholtz-Zentrum Berlin, Hahn-Meitner-Platz 1, 14109 Berlin — [2]Helmholtz-Zentrum Berlin, Hahn-Meitner-Platz 1, 14109 Berlin

We investigate the adsorption of proteins on a partially-charged and end-grafted polyelectrolyte brush using explicit-water and coarse-grained computer simulations and Poisson-Boltzmann theory. The effects of the salt concentration, grafting density, and the charge fraction of the brushes on brush profiles and protein adsorption free energies are calculated and compared to approximative analytical theories.

BP 7.32   Mon 17:30   Poster A

Divalent cation force field optimization based on thermodynamic properties
— •Shavkat Mamatkulov[1], Maria Fyta[2], and Roland R. Netz[1] — [1]Fachbereich Physik, Freie Universität Berlin, 14195 Berlin, Germany — [2]Physik Department, Technische Universität München, 85748 Garching, Germany

In this work we develop force field parameters of the divalent cations Mg^{2+}, Ca^{2+}, Ba^{2+}, and Sr^{2+}. We perform Molecular Dynamics simulations with explicit water, using the SPC/E water model. The scheme we propose for the derivation of the ionic force fields is based on a simultaneous optimization of single-ion and ion-pair properties. The solvation free energy and the effective radius of the divalent cations are the single ion properties used in our approach. As a probe for the ion pair properties we compute the activity derivatives of salts in aqueous solutions. The optimization of the ionic force fields was done in two distinct steps. First, the solvation free energy and the first maximum in the ion-water radial distribution function (RDF) were determined as a function of the Lennard-Jones (LJ) parameters used in the simulations. Second, knowledge of the combinations of the LJ parameters which reproduce the exact solvation free energy and the first peak in the RDF of the divalent cations allowed us to compute the activity derivatives of the electrolytes such as MgY_2, CaY_2, BaY_2, SrY_2, where $Y=Cl^-$, Br^-, I^-.

BP 7.33   Mon 17:30   Poster A

Single Peptide Desorption from Solid Surfaces — •Susanne Liese[1], Nadine Schwierz[2], and Roland Netz[1] — [1]FU Berlin, Germany — [2]TU Munich, Germany

The desorption of single homopeptides from solid surfaces is examined by molecular dynamic (MD) simulations and analytical calculations. To investigate the role of the surface hydrophobicity on peptide desorption, the relation between the hydrophobicity of a self-assembled monolayer (SAM) with non-polar terminal groups and the force necessary to desorb different homopeptides from such surfaces is investigated by MD simulations. For the purely non-polar surfaces the desorption force decreases with increasing surface hydrophobicity and increases with increasing peptide hydrophobicity. Additionally, the equilibrium and non-equilibrium effects of the finite polymer length on the forced desorption of single polymers by AFMs, is examined in the framework of a freely jointed chain and a worm-like chain-model. With these rather simple models experimental observations from the group of Prof. Thorsten Hugel at TU Munich are successfully described, such as the dependency between rupture length and desorption force. Furthermore, the question, to which extent the desorption process is reversible, is addressed.

BP 7.34   Mon 17:30   Poster A

Single molecule force spectroscopy of desmoglein-2-homocomplexes — •Verena Mohaupt[1], Volker Walhorn[1], Anna Gärtner[2], Hendrik Milting[2], and Dario Anselmetti[1] — [1]Experimental Biophysics & Applied Nanoscience, Bielefeld University, Germany — [2]E. & H. Klessmann Institute for Cardiovascular Research & Development, Heart and Diabetes Centre NRW, Ruhr-University Bochum, Bad Oeyenhausen, Germany

Desmosomes are molecular complexes of cell-adhesion molecules and linking proteins that form the junction between adherent cells like heart muscle cells. These domains exhibit a high density of Ca^{2+}-dependent cell adhesion proteins like desmoglein (DSG) or desmocollin (DSC). Notably, mutations in desmosomal proteins are often associated with inherent heart muscle disease like arrhythmogenic right ventricular cardiomyopathy (ARVC), which is the major cause of sudden cardiac death in adolescent and athletes.

We use atomic force microscopy (AFM) and AFM single molecule force spectroscopy (AFM-SMFS) to investigate and quantify the Ca^{2+}-dependent bond strength of single DSG2-homocomlexes. Furthermore binding kinetics and reaction lengths can be deduced according to the Kramers-Bell-Evans model. The analysis and comparison of wildtype and mutant DSG2 with respect of insights to the processes of ARVC related heart muscle degeneration will be discussed.

BP 7.35   Mon 17:30   Poster A

Peptide Dynamics Simulations in Light and Heavy Water: Zooming in on Internal Friction — •Julius Christoph Friedrich Schulz Schulz[1], Lennart Schmidt[1], Joachim Dzubiella[2], and Roland Netz[1] — [1]Fachbereich Physik, Freie Universitaet Berlin, 14195 Berlin, Germany — [2]Helmholtz Zentrum Berlin fuer Materialien und Energie, 14109 Berlin, Germany

Frictional effects due to the chain itself, rather than the solvent, may have a significant effect on protein dynamics. Experimentally, such "internal friction" has been investigated by studying folding or binding kinetics at varying solvent viscosity; however the molecular origin of these effects is hard to pinpoint. We consider the kinetics of disordered glycine-serine and alpha-helix forming alanine peptides, and a coarse-grained protein folding model in explicit-solvent molecular dynamics simulations. By varying the solvent mass over more than two orders of magnitude, we alter only the solvent viscosity and not the folding free energy. Folding dynamics at the near-vanishing solvent viscosities accessible by this approach suggest that solvent and internal friction effects are intrinsically entangled. This finding is rationalized by calculation of the polymer end-to-end distance dynamics from a Rouse model that includes internal friction. An analysis of the friction profile along different reaction coordinates suggests a connection between friction and the formation of hydrogen bonds upon folding.

BP 7.36   Mon 17:30   Poster A

Free Energy Landscape for Entrance Pathway of CoA into the Active Site of Pyruvate-Formate-Lyase — •Karmen Čondić-Jurkić[1,2], Ana-Sunčana Smith[1], and David M. Smith[2,3] — [1]Institut für Theoretische Physik, Universität Erlangen-Nürnberg, Erlangen, Germany — [2]Rudjer Bošković Institute, Zagreb, Croatia — [3]Computer-Chemie-Centrum, Universität Erlangen-Nürnberg, Erlangen, Germany

Knowledge of how free energy of a certain process changes along the reaction coordinate has always been of great interest, both in chemistry and physics. Therefore, a lot of effort has been made in the direction of developing methods and computational tools to estimate potential of mean force. Several such methods implemented in the AMBER software package were used in the search of the possible entrance pathways of a ligand (CoA) into the active site of the protein (Pyruvate-Formate-Lyase). The conformational space of the system was explored by the umbrella sampling method and its variation, so called targeted MD. The latter method allows somewhat greater flexibility in the choice of the possible pathway by defining the reaction coordinate as structural RMS deviation between the final and initial conformation and could give rise to alternative pathways. As a complementary approach to these equilibrium methods, we have used steered dynamics to study the process by exposing it to non-equilibrium conditions, i.e. by doing the pulling experiments and using Crooks fluctuation theorem to extract the information about the free energy profile. Finally, the PMF obtained from all three approaches will be compared and discussed.

BP 7.37   Mon 17:30   Poster A

Investigation of desmin intermediate filament assembly by atomic force microscopy — •Mareike Dieding[1], Volker Walhorn[1], Andreas Brodehl[2], Hendrik Milting[2], and Dario Anselmetti[1] — [1]Experimental Biophysics & Applied Nanoscience, Bielefeld University, Germany — [2]E. & H. Klessmann Institute for Cardiovascular Research & Development, Heart and Diabetes Centre NRW, Ruhr-University Bochum, Bad Oeynhausen, Germany

Intermediate filament (IF) proteins form extended filamentous networks in metazoan cells. Desmin IF is a vital structural component of the cytoskeleton in myocytes. In line with the functional importance of desmin, we investigated several desmin mutants associated with the

inherited heart muscle disease arrhythmogenic right ventricular cardiomyopathy (ARVC), which is a major cause of sudden cardiac death in adolescent and athletes.

Using atomic force microscopy (AFM), we studied desmin oligomers at different stages of the *in vitro* assembly process. Thereby we were able to reveal various mutation specific structural defects at distinct stages of the filament assembly. These findings are nicely supported by complementary methods like cell transfection studies [1,2].

[1] A. Brodehl et al., *Dual-color photoactivation localization microscopy of cardiomyopathy associated desmin mutants*, submitted.

[2] B. Klauke et al., *De novo desmin-mutation N116S is associated with arrhythmogenic right ventricular cardiomyopathy*, Hum. Mol. Genet. 19(23), 2010.

BP 7.38 Mon 17:30 Poster A

SMS - FRET spectroscopy has emerged as a versatile tool in life sciences. — •Phillip Kroehn and Jörg Enderlein — Drittes Physikalisches Institut Göttingen

The applications range from protein-protein interactions and imaging microscopy to fast dynamic processes such as protein folding.

For SMS-FRET measurements in protein folding studies, site specific labelling of the protein with a donor and acceptor dye is limited to the reaction of cystein and lysine residues. Depending on the site of the protein two approaches overcome the uncertainty of random labelling.

1)*For small proteins or peptides up to 50 aa, solid phase peptide synthesis (SPPS) is the method of choice. By using aa with different protective groups site specific coupling to virtual all residues is possible.

2)*For larger proteins two new evolving methods enable the site specific coupling of dyes: a) the so called orthogonal-system allows the insertion of unnatural aa via bacterial expression in the polypeptide chain, the dye is then specifically coupled to the functional side chain of the unnatural aa. (Schulz et al J Am. Chem. Soc., 2008). b) Intein mediated protein ligation can be used to efficiently fuse short peptides with attached fluorophores to expressed proteins (Grant et al, Biol. Chem., 2006).

BP 7.39 Mon 17:30 Poster A

Structural properties of Salvinorin A, an entheogenic substance which may become a psychotherapeutic compound — •Davoud Pouladsaz[1], Azadeh Ebrahimi[2], and Hermann Schluesener[2] — [1]Department of Biological Physics, Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Department of Neuropathology, Faculty of Medicine, University of Tübingen, Tübingen, Germany

Salvinorin A is the main active psychotropic compound in Salvia divinorum, a Mexican plant which has a long history of use as an entheogen by indigenous Mazatec shamans in Oaxaca and has gained popularity as a recreational hallucinogen for the inhalation of its pyrolyzed smoke. The potent psychotropic effects of Salvinorin A, unlike many other hallucinogenic compounds that are mediated by the serotonin receptor 5-HT$_{2A}$, are exerted through the activation of κ-Opioid receptors which are widely distributed throughout the central and peripheral nervous systems and in other tissues. The basic mechanisms behind these effects are particularly remarkable, because Salvinorin A is a non-nitrogenous κ-Opioid receptor agonist. Since the structural properties of Salvinorin A play an important role in ligand affinity and selectivity of κ-Opioid receptor, we use molecular docking techniques to identify and study the active sites of the κ-Opioid receptor in interaction with Salvinorin A. The results may improve our understanding of how novel compounds for treatment of perceptual distortions may be derived from Salvinorin A.

BP 7.40 Mon 17:30 Poster A

Biological applications for nano-mechanical detection of molecular recognition — •Andreas Mader[1], Kathrin Gruber[1], Roberto Castelli[2], Peter H. Seeberger[2], Joachim O. Rädler[1], and Madeleine Leisner[1] — [1]LMU München, Fakultät fuer Physik — [2]Department of Biology, Chemistry and Pharmacy, Freie Universität Berlin

Advances in carbohydrate sequencing technologies have revealed the tremendous complexity of the glycome. Understanding the biological function of carbohydrates requires the identification and quantification of carbohydrate interactions with biomolecules. The increasing importance of carbohydrate-based sensors able to specifically detect sugar binding molecules or cells, has been shown for medical diagnostics and drug screening. Our biosensor, with a self-assembled mannoside sensing layer, specifically detects carbohydrate-protein binding interactions (mannoside - ConA), as well as real time interaction of carbohydrates with different E. coli strains in solution. Binding to the cantilever surface causes mechanical surface stress, that is transduced into a mechanical force and cantilever bending. The degree and duration of cantilever deflection correlates with the interaction's strength. In this study we present carbohydrate-based cantilever biosensors as a robust, label-free, and scalable method to analyze carbohydrate-protein and carbohydrate-bacteria interactions. The cantilevers thereby exhibit specific and reproducible deflection with a high sensitivity range of over four orders of magnitude.

BP 7.41 Mon 17:30 Poster A

Dynamic force spectroscopy on fluorescence labeled tau-peptides and monoclonal antibodies measured by using Optical Tweezers — •Tim Stangner, Carolin Wagner, David Singer, Christof Gutsche, Olaf Ueberschär, Ralf Hoffmann, and Frierich Kremer — Uni Leipzig, Leipzig, Germany

Since humans become older and older with the fast evolution of medicine, degenerative diseases edge ever closer to focus of research. Especially Alzheimer's disease is the most common form of dementia. Each Alzheimer patient shows two commonly known changes in the brain: senile plaques of β-amyloid-peptide and tangles of hyperphosphorylated tau proteins. Dynamic force spectroscopy (DFS) is performed by using optical tweezers on the level of single receptor-ligand-interactions. Here we report about the specific binding of two anti-human tau-monoclonal antibodies (mAbs), HPT-104 and HPT-110, interacting with synthetic (non-)fluorescence-labeled tau-peptides with different phosphorylation pattern. The fluorescent tagged tau-peptides, anchored on Melanmin-resin beads, are presorted with the fluorescence activated cell sorting (FACS) method in order to achieve homogenous surface coverage. Specific binding events between peptide and mAbs are described according to the Dudko-Hummer-Szabo-model [1]. A comparison between labeled and non-labeled tau-peptide and their interactions with mAbs shall show the influence of the linker-(PEG-spacer) and the fluorescein-molecule on the parameters, obtained by the Dudko-Hummer-Szabo-model [1].

References: [1] Dudko et al.; PNAS 2008 vol. 105 no. 41 15755-15760

BP 7.42 Mon 17:30 Poster A

Modeling the Light-Dependent Repression of Photosynthesis Genes by the AppA/PpsR System in Rhodobacter sphaeroides — •Rakesh Pandey[1], Dietrich Flockerzi[1], Marcus J. B. Hauser[2], and Ronny Straube[1] — [1]Max Planck Institute for Dynamics of Complex Technical Systems, Magdeburg — [2]Institute of Experimental Physics, Otto-von-Guericke University, Magdeburg

Purple bacteria derive energy from aerobic respiration or photosynthesis (PS) depending on the availability of oxygen and light. Under aerobic conditions, PS genes are specifically repressed by the PpsR protein. In R. sphaeroides, the repressive action of PpsR is antagonized by the blue-light sensitive flavoprotein AppA which forms transcriptionally inactive complexes with PpsR under anaerobic conditions. However, under semi-aerobic conditions blue-light excitation of AppA causes the AppA-PpsR complexes to dissociate leading, again, to PS gene repression. We have recently proposed a simple mathematical model [1] which suggests that this phenotype arises from the formation of a maximum in the response curve of PpsR at intermediate oxygen levels. Here, we present an extended model which incorporates a more realistic mechanism for the light regulation. Its predictions compare favorably with experimental results on the light-dependent repression of PS genes under semi-aerobic conditions. We also identify potential kinetic and stoichiometric constraints that the interplay between light and redox regulation imposes on the functionality of the AppA/PpsR system, especially with respect to a possible bistable response. [1] Pandey R, Flockerzi D, Hauser MJB, Straube R. Biophys. J. 100, 2347 (2011).