BP 33: Protein Structure and Dynamics

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

BP 33.1 Thu 9:30 ZEU 250

Protein Short-Time Diffusion in a Naturally Crowded Environment — Marco Grimaldo[1], Hender Lopez[1,2,3], •Christian Beck[1,2], Olga Matsarskaia[1], Felix Roosen-Runge[5], Martine Moulin[1], Juliette Devos[1], Valerie Laux[1], Michael Hartlein[1], Stefano Da Vela[2], Ralf Schweins[1], Alessandro Mariani[4], Fajun Zhang[2], Jean-Louis Barrat[3], Martin Oettel[2], V. Trevor Forsyth[1,6], Tilo Seydel[1], and Frank Schreiber[2] — [1]Institut Laue-Langevin, Grenoble, France — [2]University of Tübingen, Germany — [3]LiPhy, Saint Martin d'Hères, France — [4]European Synchrotron Radiation Facility, Grenoble, France — [5]Malmö University, Malmö, Sweden — [6]Keele University, Staffordshire, UK

We employ neutron backscattering spectroscopy to measure the short-time self-diffusion of tracer proteins in a deuterated cell-like environment (cell lysate) with explicit control over crowding conditions. We successfully link coarse-grained Stokesian dynamics simulations with experimental results on these complex, flexible molecules providing a consistent understanding by colloid theories. In the case of immunoglobulin, both experiments and simulations show that tracers in polydisperse solutions close to the effective particle radius $R_{eff} = \langle R_i^3 \rangle^{1/3}$ diffuse approximately as if the suspension was monodisperse [1]. The simulations predict size-dependent deviations from this scaling which was tested by measuring different proteins in lysate with an increased energy transfer range, also allowing to investigate the influence of the lysate on the internal dynamics in more detail. [1] M. Grimaldo *et al.*; J. Phys. Chem. Lett. 10 (2019) 1709

BP 33.2 Thu 9:45 ZEU 250

Conformational Changes of IDP under Influence of Guanidinium Chloride: Integrative Approach using X-ray/Neutron Scattering and Single Molecule Spectrosopy — •Luman Haris[1,2], Livia Balacescu[1,2,3], Iwo König[4], Martin Dulle[1], Aurel Radulescu[3], Ingo Hoffmann[5], Tobias Erich Schrader[3], Ben Schuler[4], and Andreas Maximilian Stadler[1,2] — [1]FZ Jülich, JCNS-1 & ICS-1, Jülich — [2]IPC, RWTH Aachen, Aachen — [3]FZ Jülich, Outstation MLZ, Garching — [4]Biochemisches Institut, Universität Zürich, Zürich — [5]Institut Laue-Langevin, Grenoble

IDPs are identified by the presence of unfolded region due to relatively abundant polar residues content within its amino acid sequence. Together with other residues, IDPs exhibit not only high flexibility but also sensitivity to physico-chemical fluctuation such as pH, temperature, and ions concentration. For this reason, IDPs are involved in cellular processes such as DNA repair scheme and chromatin modification. In this project, we pursue a quantitative description of structure and dynamics of IDPs with different net charges: namely Prothymosin Alpha and Myelin Basic Protein. Here, we employed neutron spin-echo spectroscopy (NSE) and small angle X-ray scattering (SAXS) to gain insight on the emergence of internal friction within the peptide and its conformational change as a function of Guanidinium Chloride (GndCl) concentration respectively. The experimental results obtained from SAXS shows contraction and expansion as measured by FRET. Similarly, from NSE data, we are able to extract the internal friction which is in good agreement with FCS result.

BP 33.3 Thu 10:00 ZEU 250

Electronic Quantum Coherence in Photosynthetic Protein Complexes — •Hong-Guang Duan[1], Ajay Jha[1], Vandana Tiwari[1], Richard J. Cogdell[2], Khuram Ashraf[2], Valentyn I. Prokhorenko[1], Michael Thorwart[3], and R. J. Dwayne Miller[1,4] — [1]MPSD, Hamburg — [2]Institute of Molecular, Cell & Systems Biology, University of Glasgow, UK — [3]I. Institut für Theoretische Physik, UH, Germany — [4]University of Toronto, Canada

Quantum mechanics was initially developed in the field of atomic physics and rapidly extended to quantum chemistry in the early 20th century. The extension of seeking quantum effects in biological systems is of one of the important areas of research, termed as quantum biology. Recent experimental studies reported long-lived quantum coherence in the primary step of energy transfer in photosynthetic protein complexes. However, the origin of the coherence is still under debate. To capture the solid evidence of electronic quantum coherence, we studied the quantum dynamics in Fenna-Matthews-Olson (FMO) complex by two-dimensional (2D) electronic spectroscopy at different temperatures. We clearly observed the electronic coherence with time scale of 500 fs at low temperature (20 K). However, the lifetime of electronic coherence is dramatically reduced with increasing of temperature. We observed, at room temperature, the electronic coherence is too short (~60 fs) to play any functional role in the process of energy transfer in FMO complex. Moreover, we identified that the long-lived oscillations in 2D spectra are mainly contributed by Raman modes on the electronic ground states.

BP 33.4 Thu 10:15 ZEU 250

Following the formation of PYP's photocycle intermediates on a femtosecond to millisecond timescale with a site-specific IR label — •Larissa Blankenburg, Luuk J.G.W. van Wilderen, and Jens Bredenbeck — Goethe-Universität, Institut für Biophysik, Max-von-Laue-Str. 1, 60438 Frankfurt am Main, Germany

The photocycle dynamics of Photoactive Yellow Protein (PYP) that are induced by excitation with blue light occur on a timescale ranging from femtoseconds to seconds. Local dynamic information about the protein can be obtained by the use of the vibrational label thiocyanate (SCN) that can be inserted site-specifically at any desired position by cysteine mutation and cyanylation. The CN stretch vibration is highly sensitive to polarity and hydrogen-bonding interactions and thus allows to probe local structural changes during PYP's photocycle.

With transient fs-ms infrared spectroscopy on SCN-labeled PYP mutants we followed most part of the photocycle from chromophore isomerization (ps) and protonation (μs) to partial unfolding of the protein (ms). The data revealed spectral changes corresponding to alterations in the local environment of the non-perturbing label, providing dynamic site-specific structural information for multiple observed photocycle intermediates. While the site resolution in infrared spectroscopy of unlabeled proteins is generally limited to a few marker bands (e.g. of the chromophore or specific side chains), vibrational labels can be inserted at almost every location improving the structural resolution and investigation of proteins and may resolve new intermediates.

Invited Talk BP 33.5 Thu 10:30 ZEU 250

Atomistic ensembles of proteins and soft matter complexes from MD simulations and solution scattering data — Milos T Ivanovic[1], Markus R Hermann[2], and •Jochen S Hub[1] — [1]Unvierstität des Saarlandes, Saarbrücken, Germany — [2]Georg-August-Universität Göttingen, Germany

Understanding the function of disordered peptides or soft-matter complexes requires understanding of their conformational ensembles. However, experimental data alone is often insufficient for defining all degrees of freedom of such systems, whereas simulations may be biased by poor sampling or force field limitations. We developed a method for coupling atomistic simulations to small- and wide-angle X-ray scattering (SAXS/WAXS) data, based on Jaynes' principle of maximum entropy, with the aim to obtain accurate atomistic ensembles biomolecular and soft-matter systems. As examples, we show that the method is capable of overcoming force field inaccuracies in simulations of an intrinsically disordered protein and of a detergent micelle. In addition, we critically review capabilities and limitations of widely used continuum models in deriving micellar structures.

[1] Hub, Curr Opin Struct Biol, 49, 18-26 (2018)
[2] Hermann and Hub, J Chem Theory Comput, 15, 95103-5115 (2019)
[3] Ivanović, Bruetzel, Lipfert, Hub, Angew Chem Int Ed, 57, 5635-5639 (2018)
[4] Ivanović, Hermann, Wójcik, Pérez, Hub, BioRxiv doi:10.1101/815266

30 min. coffee break

BP 33.6 Thu 11:30 ZEU 250

van der Waals Forces in Biomolecular Systems: from Solvation to Long-range Interaction Mechanisms — •Martin Stöhr and Alexandre Tkatchenko — Physics and Materials Science Research Unit, University of Luxembourg

A decisive characteristic of the biomolecular machinery is the access to a rich set of coordinated processes within a small energy window. Most of these processes involve collective conformational changes and occur in an aqueous environment. Conformational changes of (bio)molecules

as well as their interaction with water are thereby largely governed by non-covalent van der Waals (vdW) dispersion interactions. By virtue of their intrinsically collective nature, vdW forces also represent a key influence on collective nuclear behavior. Our understanding of vdW interactions in large-scale (bio)molecular systems, however, is still rather limited [Chem. Soc. Rev. 2019, 48, 4118]. Here, we employ the Many-Body Dispersion framework to investigate the vdW interaction in biomolecular systems and its spatial and spectral aspects. In particular, we show the role of beyond-pairwise vdW forces for protein stability and highlight the delocalized character of the protein-water vdW interaction. We further examine intermolecular electronic behaviors and reveal a coexistence of strong delocalization with spatially-separated, yet correlated, local domains. This, ultimately, forms the basis for a potential, efficient long-range interaction mechanism for coordinated processes in biomolecular systems.

BP 33.7 Thu 11:45 ZEU 250

Investigating the conformational ensembles of intrinsically-disordered proteins with a simple physics-based model — •Yani Zhao, Robinson Cortes-Huerto, Kurt Kremer, and Joseph F. Rudzinski — Max Planck Institute for Polymer Research, Mainz, Germany

The coupled interactions of intrinsically disordered proteins (IDPs) with its partners play an important role in biological processes but present a number of fundamental challenges for computational modeling. This challenge is magnified for proteins due to the variety of competing interactions and large deviations in side-chain properties. In this work, we apply a simple physics-based coarse-grained model for describing largely disordered conformational ensembles of peptides, based on the premise that sampling sterically-forbidden conformations can compromise the faithful description of both static and dynamical properties. The Hamiltonian of the employed model can be easily adjusted to investigate the impact of distinct interactions and sequence specificity on the randomness of the resulting conformational ensemble. Starting with a bead-spring-like model and then adding more detailed interactions one by one, we construct a hierarchical set of models and perform a detailed comparison of their properties. Our analysis clarifies the role of generic attractions, electrostatics and side-chain sterics, while providing a foundation for developing efficient models for IDPs that retain an accurate description of the hierarchy of conformational dynamics, which is nontrivially influenced by interactions with surrounding proteins and solvents.

BP 33.8 Thu 12:00 ZEU 250

Comparison of continuous and discrete Markov models of biomolecular dynamics — •Benjamin Lickert and Gerhard Stock — Universität Freiburg

Motions of biomolecular systems, recorded by molecular dynamics simulations, are often modeled as Markov processes. A very popular approach is given by Markov state models where the conformational space is divided into different states [1]. To be Markovian, the intrastate dynamics need to be significantly faster than the interstate dynamics. On the other hand, the observed dynamics can be modeled as a continuous diffusive process, called Langevin dynamics, on some low-dimensional free energy landscapes $F(\vec{x})$. In this case, Markovianity is given if the system, i.e., $\vec{x}(t)$, evolves substantially slower than the neglected degrees of freedom, i.e., the bath surrounding the system. Recently, a data-driven approach was formulated to estimate such a Langevin model from a given trajectory $\vec{x}(t)$ [2]. Here, we compare the features of both modeling frameworks. While Markov state models are very appealing due to their clearly structured generation and interpretation, Langevin dynamics have the advantage that they allow for the estimation of continuously defined observables, like free energy and autocorrelations. Using molecular dynamics simulations of systems with varying complexity we have a look at these points in practice.

[1]: J.H.Prinz et al., J.Chem.Phys. 134, 174105 (2011)
[2]: N.Schaudinnus et al., J.Chem.Phys. 145, 184114 (2016)

BP 33.9 Thu 12:15 ZEU 250

Hybrid Kinetic Monte Carlo / Molecular Dynamics Simulations of Bond Scissions in Proteins — •Benedikt Rennekamp[1,2] and Frauke Gräter[1,2] — [1]Heidelberg Institute for Theoretical Studies, Schloss-Wolfsbrunnenweg 35, 69118 Heidelberg, Germany — [2]Interdisciplinary Center for Scientific Computing, Heidelberg University, INF 205, 69120 Heidelberg, Germany

Proteins are exposed to various mechanical loads that can lead to covalent bond scissions even before macroscopic failure occurs. In regular Molecular Dynamics (MD) simulations covalent bonds are, however, predefined and reactions cannot occur. Furthermore, such events rarely take place on MD time scales.

We have developed a hybrid Kinetic Monte Carlo / Molecular Dynamics (KIMMDY) scheme that overcomes the separation of time scales of these processes and drastically increases the accessible time scales for reactive MD simulations. Here, bond rupture rates are calculated in the spirit of a transition state model based on the interatomic distances in the MD simulation and then serve as an input for a Kinetic Monte Carlo step.

With this new technique we investigated bond ruptures in a multi-million atom system of tensed collagen, a structural protein found in skin, bones and tendons. Our simulations show a clear concentration of homolytic bond scissions near chemical crosslinks in collagen. We suggest that these created mechanoradicals are a yet unknown connection converting mechanical into oxidative stress. This application also demonstrates the scalability of our hybrid computational approach.

BP 33.10 Thu 12:30 ZEU 250

Watching an enzyme at work: Time-Resolved Serial Crystallography reveals water mediated allosteric regulation — •Henrike Müller-Werkmeister — Uni Potsdam, Institut für Chemie, Physikalische Chemie, Karl-Liebknecht-Str. 24-25, 14476 Potsdam

We have studied the homodimeric enzyme fluoroacetate dehalogenase by time-resolved serial synchrotron crystallography (TR-SSX). Using a fixed target based sample delivery [1] with an efficient interlacing pattern allowed us to realize "hit-and-return" (HARE) TR-SSX to cover the full timescale from 30 milliseconds to 30 seconds [2]. With a photocaged substrate for reaction initiation, four catalytic turnovers could be resolved [3]. The total of 18 independent structures not only provide unprecedented insight into the reaction mechanism, showing the substrate binding, the Michaelis-Menten-complex and the covalent intermediate, but also reveal the allosteric mechanism leading to half-the-sites reactivity. In fact, a molecular water wire can be observed that together with molecular breathing is clocked to the enzymatic reaction.

[1] I. Martiel, H. M. Müller-Werkmeister, A. E. Cohen, Acta Cryst. D, 2019, D75, 160*177 [2] E. C. Schulz*, P. Mehrabi*, H. M. Müller-Werkmeister*, F. Tellkamp, A. Jha, W. Stuart, E. Persch, R. De Gasparo, F. Diederich, E. F. Pai, R. J. D. Miller, Nature Methods, 2018, 15 (11), 901-904 [3] P. Mehrabi*, E. C. Schulz*, R. Dsouza, H. M. Müller-Werkmeister, F. Tellkamp, R. J. D. Miller, E. F. Pai, Science, 2019, 365 (6458), 1167-1170

BP 33.11 Thu 12:45 ZEU 250

Control of (bio)nanoparticles with external fields — •Jannik Lübke[1,2,3], Lena Worbs[1,3], Armando Estillore[1], Amit Kumar Samanta[1], and Jochen Küpper[1,2,3,4] — [1]Center for Free-Electron Laser Science, Deutsches Elektronen-Synchrotron DESY, Hamburg, Germany — [2]Center for Ultrafast Imaging, Universität Hamburg, Germany — [3]Department of Physics, Universität Hamburg, Germany — [4]Department of Chemistry, Universität Hamburg, Germany

Single-particle imaging (SPI) experiments rely on dense streams of isolated nanoparticles that are guided into the focus of free-electron lasers (FELs). Then typically diffraction data from arbitrary spatial orientations of the particles are collected, classified, combined into a three-dimensional (3D) diffraction volume and inverted to the underlying 3D structure of the sample [1].

To achieve atomic resolution, beams of many, ideally identical, particles need to be delivered into the FEL focus, which necessitates sample control methods to select nanoparticles. We develop and characterize various control techniques, such as particle beam focusing using fluid dynamics [2], temperature control [3], charge state state selectivity using electric fields [4], and further techniques. Here, we present novel approaches for the production of pure and high-density beams of a broad variety of biological nanoparticles, using external fields.

[1] M. M. Seibert et al., *Nature* **470**, 78 (2011)
[2] N. Roth et al., *J. Aerosol Sci.* **124**, 17 (2018)
[3] A. K. Samanta et al. *arXiv*:1910.12606 (2019)
[4] Y. P. Chang et al., *Int. Rev. Phys. Chem.* **34**, 557 (2015)