BP 2: Protein Structure & Dynamics

Time: Monday 10:15–13:00 Location: ZEU 260

Invited Talk BP 2.1 Mon 10:15 ZEU 260

Protein Structure and Dynamics from Low-Resolution Data — •Gunnar F. Schröder — Forschungszentrum Jülich

Structure determination of large proteins and protein assemblies is a major challenge in molecular biology. Experiments, such as X-ray crystallography or single particle Cryo-EM, on such complex systems often yield only low resolution (> 4Å) data, which are not sufficient to fully determine atomistic structures. The refinement of approximate initial models is typically significantly harder than at high resolution. We present an approach that makes use of additional prior information on homologous structures which guides the refinement and dramatically improves the obtained structures.

Single-particle Cryo-EM yields images of individual proteins in potentially different conformations and therefore yields a wealth of information on structural dynamics. This information is however very difficult to extract since each image is extremely noisy. The common approaches to reconstruct three-dimensional density maps average out any structural heterogeneity and the information on the dynamics is lost. We show how principal protein motions can be reconstructed from the variation contained in the single particle images.

BP 2.2 Mon 10:45 ZEU 260

Mechanism of signal transduction of the LOV2-Jα-photosensor from Avena sativa — •Emanuel K. Peter, Bernhard Dick, and Stephan A. Baeurle — Fakultaet für Chemie und Pharmazie, Universitaet Regensburg, 93040 Regensburg, Deutschland

Fusion proteins containing light-activable protein domains possess great potential as molecular switches in cell signaling and for controlling enzymatic reactivity. This has recently been impressively demonstrated in living cell experiments through connecting the blue light-activable LOV2-Jα-protein domain from phototropin1 of Avena sativa (AsLOV2-Jα) with the Rac1-GTPase, responsible for regulating the morphology and motility of metazoan cells. However, a target-oriented development of fusion proteins in conjunction with the AsLOV2-Jα-photosensor is still very challenging, because a detailed understanding of its signal transduction pathway on a molecular level is still lacking. In this presentation we elucidate the mechanism of signal transduction of this photosensor on a molecular level, which opens new perspectives for the creation of light-activable molecular switches and enzymes [1].

[1] E. Peter, B. Dick and S. A. Baeurle, Nature Communications 1 : 122 (2010); doi: 10.1038/ncomms1121 (2010)

BP 2.3 Mon 11:00 ZEU 260

Concurrent Enzymatic Reactions as a Source of Bistability in Single Protein Modification Cycles — •Ronny Straube — MPI for Dynamics of Complex Technical Systems, Magdeburg, Germany

It is well known that reversible protein modifications can generate ultrasensitivity when the modifying enzymes operate in saturation [1]. They can also exhibit bistability if the substrate protein is antagonistically modified at multiple sites [2]. However, in the mathematical description of such mechanisms it is often neglected that the activity and/or substrate affinity of the modifying enzymes (e.g. kinase and phosphatase) is often itself regulated through reversible binding of allosteric effectors which can inter convert the respective enzyme species between a high and a low catalytic activity form. Here, I show that the concurrent action of such different activity forms of an antagonistic enzyme pair can generate a bistable system response already at the level of a single protein modification cycle, i.e. without the requirement for multisite modifications. In contrast to other mechanisms [1,2] bistability is predicted to occur even when substrate molecules and enzymes are present in equal amounts. I further show that the same mechanism is also applicable to two component systems which are the most simple signal transduction systems in bacteria. Since the formation of enzyme sub populations is difficult to avoid both *in vivo* and *in vitro* concurrent enzymatic reactions might be a ubiquitous source for generating bistability in biological systems. [1] A. Goldbeter and D. E. Koshland Jr. *PNAS* **78**, 6840 (1981). [2] N. I. Markevich, J. B. Hoek and B. N. Kholodenko *J. Cell Biol.* **164** 353 (2004).

BP 2.4 Mon 11:15 ZEU 260

Lateral Diffusion and Correlation of Membrane Anchored Proteins — •Wasim Abuillan[1], Andreas Hartel[2], Nicola Jones[2], Markus Engstler[2], and Motomu Tanaka[1] — [1]Institute for Physical Chemistry, Heidelberg University, Germany — [2]Department of Cell and Developmental Biology, Würzburg University, Germany

Many Glycosylphosphatidylinositol (GPI) - anchored proteins are found on the plasma membrane.e.g. ~ 0.5 % of cellular proteins in eukaryotes are GPI-anchored. For example, GPI-anchored Variant Surface Glycoprotein (VSG) is among the most abundant cell-surface proteins in trypanosoma protozoa, playing important roles in viability and defense against the host immune system. The lateral mobility of lipids and membrane proteins is essential for them to maintain their function. The lateral correlation and coupling of membrane proteins are studied by Grazing Incidence Small Angle X-ray Scattering (GISAXS) and high energy X-ray reflectivity (XRR) at the air/water and solid/water interfaces. Although this has been a challenge due to the low contrast in the scattering length density of proteins, we have successfully detect the two membrane anchored proteins using XRR and GISAXS: (i) engineered recombinant avidin coupled to biotinylated lipids, and (ii) GPI-anchored VSG purified from trypanosoma. XRR results revealed the uniform coupling/incorporation of proteins to the membrane surface, while the form- and structure factors of the proteins in the plane of membranes have been determined by GISAXS.

15 min. break

BP 2.5 Mon 11:45 ZEU 260

Using Graph Measures to Observe Complex Formation in Multiparticle Simulations — Florian Lauck[1,2] and •Tihamer Geyer[1] — [1]Center for Bioinformatics, Saarland University, Saarbrücken — [2]Dep. of Bioengineering and Therapeutic Sciences, UC San Francisco, CA, USA

Modern simulation techniques are beginning to study the dynamic assembly and disassembly of multi-protein systems. In these many-particle simulations it can be very tedious to monitor the formation of specific structures such as fully assembled protein complexes or virus capsids above a background of monomers and partial complexes. However, such analyses can be performed conveniently when the spatial configuration is mapped onto a dynamically updated interaction graph. On the example of Monte Carlo simulations of spherical particles with either isotropic or directed mutual attractions we demonstrate that this combined strategy allows for an efficient and also detailed analysis of complex formation in many-particle systems.

BP 2.6 Mon 12:00 ZEU 260

Asymmetric folding pathways and transient misfolding in a coarse-grained model of proteins — •Katrin Wolff[1], Michele Vendruscolo[2], and Markus Porto[3] — [1]Institute for Condensed Matter and Complex Systems, University of Edinburgh, UK — [2]Department of Chemistry, University of Cambridge, UK — [3]Institut für Theoretische Physik, Universität zu Köln, Germany

We investigate free energy landscapes and protein folding pathways in a coarse-grained protein model. Our model's two primary characteristics are a tube-like geometry to describe the self-avoidance effects of the polypeptide chain, and an energy function based on a one-dimensional structural representation which specifies the amino acids' connectivity for any given conformation. Such an energy function, rather than favouring the formation of specific native pairwise contacts, promotes the establishment of the native connectivity for each amino acid. Specifically, we look at the free energy landscape of the villin headpiece domain (Protein Data Bank (PDB) id. 1und) and show that in its distinctive asymmetry it resembles that found in computationally much more demanding atomistic molecular dynamics studies [1]. That the asymmetry is indeed a specific feature of the villin headpiece domain is demonstrated by studying the free energy landscape of another small three-helix bundle protein (PDB id. 1dv0), for which we find an essentially symmetric free energy landscape [2].

[1] H. Lei *et al.*, Proc. Natl. Acad. Sci. USA **104**, 4925 (2007)
[2] K. Wolff *et al.*, *submitted*

BP 2.7 Mon 12:15 ZEU 260

Impact of compatible solutes on the local water structure and the structural organization of lipid monolayers — •Jens Smiatek[1], Rakesh Kumar Harishchandra[2], Oliver Rubner[1], Hans-Joachim Galla[2], and Andreas Heuer[1] — [1]Institut für Physikalische Chemie, Westfälische Wilhelms-Universität Münster, D-48149 Münster, Germany — [2]Institut für Biochemie, Westfälische Wilhelms-Universität Münster, D-48149 Münster, Germany

We have performed Molecular Dynamics simulations of ectoine, hydroxyectoine and urea in explicit solvent. Special attention has been spent on the characteristics of the local ordering of water molecules around these compatible solutes. Our results indicate that ectoine and hydroxyectoine are able to bind more water molecules than urea on short scales. Furthermore we investigated the number and appearance of hydrogen bonds between the molecules and the solvent. The simulations show that some specific groups in the compatible solutes are able to form a pronounced ordering of the local water structure. Additionally, we have validated that the charging of the molecules is of main importance. Furthermore we show the impact of a locally varying salt concentration. Experimental results are shown which indicate a direct influence of compatible solutes on the liquid expanded-liquid condensed phase transition in DPPC monolayers. We are able to identify a variation of the local water pressure around the comaptible solutes by numerical calculations as a possible reason for an experimentally observed broadening of the phase transition.

BP 2.8 Mon 12:30 ZEU 260

Simulation of protein charge inversion by trivalent metal ion binding — •Sara Leibfarth[1], Felix Roosen-Runge[1], Fajun Zhang[1], Nina Fischer[2], Oliver Kohlbacher[2], Sophie Weggler[3], Michael Ziller[1], Andreas Hildebrandt[3], Elena Jordan[1], and Frank Schreiber[1] — [1]Institut für Angewandte Physik, Universität Tübingen — [2]Zentrum für Bioinformatik, Universität Tübingen — [3]Zentrum für Bioinformatik, Universität des Saarlandes

Experiments indicate that the effective charge of proteins in solution can be inverted by binding trivalent metal ions [1]. In addition, X-ray diffraction data show that metal ions bind to negatively charged carboxylic groups on the protein surface. In order to elucidate the binding of trivalent metal ions, two simulation approaches were carried out in the dilute protein limit for the case of Y^{3+}. Firstly, a classical protonation titration approach was adopted to trivalent ion binding [1, 2]. This approach yields binding probabilities for the binding sites of the protein. The effective charge of the protein as a function of yttrium concentration was calculated at different concentrations of monovalent salt. The results are in accordance with the experimentally observed phase transition in protein solution from the dissolved to the condensed phase. Secondly, a classical molecular dynamics simulation was performed, yielding the dynamic binding behavior of yttrium to the protein. With this approach, also the binding of several carboxylic groups to one yttrium ion is observed, which is consistent with the crystallographic findings. [1] Zhang et al., Proteins, 78:3450, 2010; [2] Zhang et al., Phys Rev Lett, 101:148101, 2008

BP 2.9 Mon 12:45 ZEU 260

Water soluble chlorophyll (Chl) binding protein (WSCP) of higher plants as model system for the investigation of pigment-pigment and pigment-protein interactions — •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 Kepler University Linz, Austria

Spectroscopic studies on pigment-pigment and pigment-protein interactions of Chl a and b bound to the recombinant class IIa WSCP from cauliflower are presented. Two Chls form a strongly excitonically coupled open sandwich dimer within the tetrameric protein matrix giving rise to an upper excitonic state with a large oscillator strength.

Fluorescence lifetime measurements show that the unusually high photostability of Chls bound to WSCP most probably originates from a diffusion barrier to interaction of molecular dioxygen with Chl triplets. The spectra are well described by a Chl dimer modulated by the protein environment. These findings are in good agreement with recent hole-burning and fluorescence line narrowing results.

The presented results illustrate the great potential of WSCP as a model system for systematic experimental and theoretical studies on the functionalizing of Chls by the protein matrix. It opens the way for the application of pigment-protein complexes as photo-switchable protein coatings of medical drugs.