BP 2: Protein Function

Time: Monday 12:15–13:15 Location: H43

BP 2.1 Mon 12:15 H43

Reduced Molecular Models in (Bio)molecular Design — •Kay Hamacher — Max-Planck-Institut fuer Physik komplexer Systeme, Dresden

Apoptosis regulating proteins play an essential role in the development of organisms, immune responses and other cellular mechanisms. The BCL-2 protein family contains the BH3 motif, which was found to be of crucial importance in e.g. cancer. The isolated, unstructured BH3-peptide can be modified by a hydrocarbon linkage to regain function as was recently shown in experiment [1] and act therefore as a pharmacological active molecule. We show how an effective, coarse-grained model can be parametrized (using molecular dynamics simulations as well as density-functional theory computations) to investigate the stability effects of such covalent cross-linking. We explain why the peptide dynamics is crucial for the proper function of the linker and the resulting folding properties of the peptide. Long range stabilization effects can be shown by time series analysis techniques as well as by information theory motivated measures. The resulting model [2] is suitable for rational design of generic cross-linking systems *in silicio*.

[1] L.D.Walensky et al. Science **305**, 1466 (2004)

[2] K.Hamacher, A.Hübsch, J.A.McCammon. J. Chem. Phys. **124**, 164907 (2006)

BP 2.2 Mon 12:30 H43

Myoglobin solvated in glycerol-water mixtures: The interplay of solvent and protein dynamics. — •Florian Kargl[1], Helen Jansson[1], Felix Fernandez-Alonso[2], and Jan Swenson[1] — [1]Department of Applied Physics, Chalmers University of Technology, SE-41296 Göteborg, Schweden — [2]Rutherford Appleton Laboratory, Chilton, Didcot OX11 0QX, *United Kingdom

Water as the most abundant substance in all living organisms is essential for the functioning of proteins and a number of other biomolecules [1]. Despite numerous investigations on the relation of the water dynamics and the protein motion [2] the coupling of the solvent and the protein dynamics is still debated [3]. Here we report on quasielastic neutron scattering (QENS) measurements on myoglobin solvated in different mixtures of water and glycerol [4]. Varying the solvent composition and using selective deuteration allows us to emphasize different dynamical processes. We discuss mean square displacements revealing the onset of solvent and protein motions on the experimental time-scale and the nature of the dynamical processes derived from the measured dynamic structure factors.

[1] H. D. Middendorf, Physica B 226, 113 (1996).

[2] D. Vitkup et al., Nature struct. biol. 7, 34 (2000); M. Tarek et al., Phys. Rev. Lett. 88, 138101 (2002); P. W. Fenimore et al., P. Natl. Acad. Sci. 99, 16047 (2002).

[3] P. W. Fenimore et al., P. Natl. Acad. Sci. 101, 14408 (2004).

[4] F. Kargl, H. Jansson, F. Fernandez-Alonso, and J. Swenson (submitted)

BP 2.3 Mon 12:45 H43

Beitrag abgesagt — •XXX XXX —

BP 2.4 Mon 13:00 H43

Molecular Dynamics and Secondary Structure Behaviour of the C-Terminus of Vinculin that includes a Membrane Binding Anchor — Gerold Diez[1], •James Smith[1], Martin Stiebritz[2], and Wolfgang Goldmann[1] — [1]LPMT — [2]LS Biotechnik,FAU Erlangen

Vinculin (1066 residues) is a focal adhesion (FA) protein and has three lipid-binding sites, residues 935-978, 1020-1040 and 1052-1066. The first two regions are amphiphatic alpha-helices identified from sequence prediction and later revealed in crystal structures. The third putative lipid-binding region is unstructured and only experimental data has demonstrated that these C-terminal residues act as an essential anchor for membrane association. Our work investigates the molecular dynamical behaviour of the last twenty-one amino acids (residues 1045-1066), represented as a polypeptide in explicit solvent. Different formal charges for one acidic and five basic residues are altered, representing different pH and salt conditions. Our findings show that the polypeptide undergoes different anti-parallel ß-sheet formation. Two mutually exclusive beta-sheets are formed between residues 1047-1058 and between residues 1057-1064. It is likely that in vivo this bi-stable secondary structure behaviour would be influenced by local changes in ionic conditions. The results suggest a mechanism for favourable lipid-binding activation of the vinculin in presence of local ionic or pH gradients. We will investigate which of these two beta-sheets form favourable hydrogen bonds with the polar heads of phospholipids membrane models.