BP 18: Single-Molecule Biophysics II

Time: Tuesday 14:00–15:15 Location: ZEU 250

Invited Talk BP 18.1 Tue 14:00 ZEU 250

Amyloid at the nanoscale: single molecule and ensemble studies of amyloid-lipid interactions — •Vinod Subramaniam — Nanobiophysics, MESA+/MIRA, University of Twente, Enschede, The Netherlands

Misfolding and aggregation of proteins into nanometer-scale fibrillar assemblies is a hallmark of many neurodegenerative diseases. Despite decades of research, the underlying biophysics remains a mystery. A particularly interesting and relevant question is the role of early aggregates in modulating the dynamics of protein nucleation and aggregation, and the mechanism of interactions of these species with lipid membranes. The transient nature, inherent heterogeneity, and low numbers of early stage aggregates necessitate single molecule spectroscopy approaches and other methods that can detect distributions of structures in ensembles.

We have worked extensively on the conformational dynamics and self-assembly of the human intrinsically disordered protein alpha-synuclein, involved in the etiology of Parkinson's disease. In this talk, I will summarize recent work using a broad repertoire of quantitative single molecule and ensemble biophysical techniques to characterize, at nanometer length scales, conformational and morphological details of alpha-synuclein amyloid nanostructures, and their interactions with lipid membranes.

BP 18.2 Tue 14:30 ZEU 250

Magnetic force driven dissociation kinetics in case-mixed protein interaction assays — •Asha Jacob, Leo J. van IJzendoorn, Arthur M. de Jong, and Menno W.J. Prins — Eindhoven University of Technology, The Netherlands

We quantify dissociation kinetics in assays with mixed specific and non-specific protein interactions. Ligand coupled superparamagnetic particles are incubated on surfaces coated with a mixture of specific receptors and non-specifically interacting proteins. Consequently, a case-mixed population of surface bound particles is formed with different binding strengths. Magnetic field gradients were used to apply translational forces on the bound complexes, either constant or increasing in time (applying a loading rate). Using a multi-component dissociation analysis, we observe case-dependent dissociation mechanisms of the particles. The classical Bell and Evans model successfully describes bond dissociation from the deep potential well of a specific bond. Bond characteristics in terms of rate constants, energy barriers and minima's in the dissociation pathway are revealed for the anti-biotin/biotin and streptavidin/biotin bond; and are in good agreement with values from SPR, other force clamp techniques, and molecular dynamics calculations. The particles bind non-specifically via interactions that show a force induced dissociation mechanism distinctly different from that of the specifically bound particles. The ability to rapidly differentiate and characterize specific and non-specific protein interactions in parallel, and affinity-rank different protein-ligand interactions on the basis of their binding pocket characteristics, will find various applications.

BP 18.3 Tue 14:45 ZEU 250

Friction dynamics of peptides at polar and non-polar surfaces — •Aykut Erbas, Dominik Horinek, and Roland R. Netz — Technische Universitaet Muenchen, Physik Department, Garcing, Germany

The friction forces and mobilities for the C_{16} spider silk and various peptides on polar and non-polar surfaces are investigated using molecular dynamics simulations. For both surfaces, the velocity dependence of the monomer mobility is determined and interpreted with non-linear analytical models. The obtained diffusion coefficients are in good agreement with experiments. It is concluded that the reason for the high friction forces on polar surfaces is hydrogen bonding. It is further shown that each hydrogen bond contributes equally to the total friction force, independent of the concentration of surface-polar groups or the type of amino acid.

BP 18.4 Tue 15:00 ZEU 250

Getting closer to the nature of specific bonds: Dynamic force spectroscopy on the binding of monoclonal antibodies and tau peptides — •Wagner Carolin[1], Singer David[2], Hoffmann Ralf[2], and Kremer Friedrich[1] — [1]Leipzig University, Department of Molecular Physics, Leipzig, Germany — [2]Leipzig University, Center for Biotechnology and Biomedicine, Leipzig, Germany

Optical tweezers-assisted dynamic force spectroscopy (DFS) is employed to investigate specific receptor/ligand-bonds on a single contact level. Here, the specific binding of two monoclonal antibodies (mAbs), HPT-110 and HPT-104, to synthetic tau-peptides with different phosphorylation pattern is analyzed. The specificity of HPT-110 to the tau-peptide containing a phosphorylation at Ser235 and of HPT-104 to the tau-peptide containing a phosphorylation at Thr231 is confirmed. Additionally, our approach allows for a detailed characterization of the unspecific interactions that are observed between HPT-104 and the peptide phosphorylated only at Ser235 and between HPT-110 and the peptide phosphorylated only at Thr231. By analyzing the measured rupture-force distributions it is possible to separate unspecific from specific interactions. Thereby for the latter characteristic parameters like the lifetime of the bond without force t0, the characteristic length xts and the free energy of activation DG are determined. The results are in accordance with conventional ELISA tests but offer a much more refined insight.