BP 12: Single Molecule Biophysics I

Time: Tuesday 9:00–11:00 Location: BPa

Invited Talk BP 12.1 Tue 9:00 BPa

Molecular simulation meets cryo electron tomography — •Gerhard Hummer — Max Planck Institute of Biophysics, Frankfurt am Main, Germany

Cryo electron tomography and molecular dynamics simulations perfectly complement each other. Electron tomograms provide us with a remarkably detailed, three-dimensional view of the molecular architecture of cells and viruses in situ, that is in the natural context; however, this view is essentially static and atomic resolution remains largely out of reach, in particular for dynamic biomolecular machineries. By contrast, molecular dynamics simulations naturally give us an atomistic view that includes dynamics, albeit in an idealized context. The synergistic potential of tomography and simulation can now be realized thanks to an increase in the resolution achievable by cryo electron tomography, a rapid growth in raw computational power, significant improvements in the quality of the potential energy functions entering classical molecular dynamics simulations, and the availability of simulation codes that can handle the complex molecular systems encountered in situ. To illustrate the power of combining molecular simulations with cryo electron tomography, I will present results from studies of the spike protein of the SARS-CoV-2 virus (Turoňová, Sikora, Schürmann et al., Science 2020) and from desmosome cell-cell junctions (Sikora, Ermel, Seybold et al., PNAS 2020).

BP 12.2 Tue 9:30 BPa

Electronic Quantum Coherence in Photosynthetic Protein Complexes — Hong-Guan Duan 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[4] — [1]Max Planck Institute for the Structure and Dynamics of Matter, Hamburg — [2]Institute of Molecular, Cell & Systems Biology, University of Glasgow, UK — [3]I. Institut für Theoretische Physik, Universität Hamburg, Germany — [4]University of Toronto, Canada

The search for quantum effects in biological systems led previous experiments to report long-lived electronic quantum coherence in the primary step of the energy transfer in photosynthetic protein complexes. However, the origin of the coherence became a topic of intense debate. We have revisited this in a joint experimental and theoretical effort studying the quantum dynamics in the Fenna-Matthews-Olson (FMO) complex by two-dimensional electronic spectroscopy at different temperatures. We found that the electronic coherence time is significantly shorter under ambient conditions than previously reported. To capture solid evidence of quantum coherence, lower temperatures are required. We have clearly observed electronic coherence with a time scale of 500 fs at low temperature (20 K). However, the coherence lifetime is rapidly reduced with increasing temperature. At room temperature, electronic coherence is too short (60 fs) to play any functional role in the energy transfer which occurs on a time scale of picoseconds. The long-lived oscillations previously reported in 2D spectra are due to Raman vibrational modes on the electronic ground state.

BP 12.3 Tue 9:50 BPa

Conformational Changes of IDP under Influence of Guanidinium Chloride: Integrative Approach using X-ray/Neutron Scattering and Single Molecule Spectrosopy — •Luman Haris[1,2], Iwo König[4], Martin Dulle[1], Aurel Radulescu[3], Ingo Hoffmann[5], Olaf Holderer[3], Tobias Erich Schrader[3], Ben Schuler[4], and Andreas Maximilian Stadler[1,2] — [1]FZ Jülich, JCNS-1 & IBI-8, 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 12.4 Tue 10:10 BPa

Do the loops in the N-SH2 binding cleft truly serve as allosteric switch in SHP2 activation? A tale of disorder, crystal contacts, and activation free energies — Massimiliano Anselmi and •Jochen S Hub — Unvierstität des Saarlandes, Saarbrücken, Germany

SHP2 is a multi-domain protein, playing an important role in upregulating cellular processes such as cell survival, proliferation, and programmed cell death. SHP2 mutations cause developmental disorders and were found in many cancer types. In healthy cells, SHP2 mainly takes an autoinhibited, inactive form, and SHP2 is activated upon binding of a phosphopeptide to the N-SH2 domain. For the past two decades, the widening of the binding cleft upon peptide binding has been considered as the key event driving SHP2 activation.

We re-analyzed the manifold amount of crystallographic data of SHP2, and we carried out extensive MD simulations and free energy calculations of SHP2 in solution and in a crystal environment. We found that the "allosteric switch" model is in fact compromised by crystal contacts and flexible, poorly resolved loops, and that the degree of openness of the binding cleft does not even influence the free energy of SHP2 opening. Instead, we detected an alternative allosteric mechanism, namely the unzipping of a central beta sheet of N-SH2, which drives SHP2 activation. Apart from the implications on SHP2 activation and inhibition, the study highlights that MD simulations in crystal and solution environments are a powerful tool to avoid misinterpretation of crystal structures.

30 min. Meet the Speaker