Intermolecular energy landscape characterization from single-molecule unbinding experiments

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Abstract:

Force-spectroscopy is a relative new-comer to an array of single molecule techniques. In this new technique, molecular reactions are driven by an external mechanical force. The resulting reaction of the molecular system is recorded as a function of the applied force. Unbinding (also known as rupture) force and force loading rate constitute the experimentally measured parameters. Existing theories connect these quantities to the parameters that characterize the intermolecular energy landscape. These energy landscape parameters include distance from the equilibrium to the transition state, activation energy, and intermolecular bond spring constant.

In this seminar, discussion of the theoretical models will be complemented with a description of the experimental force-spectroscopy technique that utilizes the force modality of atomic force microscopy. The experimental description will include essential aspects of the sample preparation, the experimental methodology, and the data analysis.

Application of the force-spectroscopy technique will be illustrated with results from single-molecule studies of disjoining of amyloidogenic peptide fragments of protein \( \alpha \)-synuclein. \( \alpha \)-Synuclein forms fibrillar aggregates known as amyloid plaque and has been connected to the etiology of neurodegenerative Parkinson’s disease and other diseases. Oligomeric species of this protein have been implicated in neurotoxicity. Details of the conformational flexibility of oligomeric species remain unclear. The single molecule force-spectroscopy measurements reveal no significant variation in the energy landscape parameters in the temperature range from 17\(^\circ\)C to 40\(^\circ\)C. Analysis of the loading rate dependence of rupture forces indicates that dimer species of the peptide fragments exhibit conformational heterogeneity.