Exploring the Configurational Landscape of Biomolecular Systems under Extreme Conditions

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Lipid bilayers, which provide valuable model systems for biomembranes, display a variety of polymorphic phases, depending on their molecular structure and environmental conditions, such as pH, ionic strength, temperature and pressure. By using spectroscopic and diffraction techniques, the temperature and pressure dependent structure and phase behaviour of simple lipid bilayers as well as binary and ternary (raft) lipid mixtures have been studied. Neutron small-angle scattering, two-photon excited fluorescence microscopy, and FT-IR spectroscopy were used to study also the lateral organization of phase-separated lipid membranes and the influence of peptide incorporation. Moreover, applying the pressure-jump relaxation technique in combination with time-resolved spectroscopic and diffraction techniques, the kinetics of various lipid phase transformations was investigated. The technique was also be applied to study other biomolecular structural transformations, such as protein folding. We present data on the pressure-induced un/refolding of various proteins. A thermodynamic approach is used for determining the stability of proteins as a function of both temperature and pressure and express it as a three-dimensional free energy surface. Morover, the effect of various chaotropic and kosmotropic cosolvents on the temperature- and pressure-dependent structure and stability of proteins is discussed. Finally, recent advances in using pressure for studying misfolding, aggregation and fibril formation (amyloidogenesis) of proteins (e.g., insulin, PrP) will be discussed.

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