Hydrophobic Hydration of Single Polymer Chains and Protein Unfolding from Hydrophobic Interfaces

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Abstract:

Hydrophobicity underpins self-assembly in many natural and synthetic molecular and nanoscale systems. Two examples will be discussed in this lecture.
In the first example, we explore hydrophobicity via its temperature dependence. The experimental evaluation of the temperature and size dependence of hydration free energy in a single hydrophobic polymer is reported, which tests key assumptions in models of hydrophobic interactions in protein folding. The hydration free energy required to extend three hydrophobic polymers with differently sized aromatic side chains was directly measured by single molecule force spectroscopy. The results are threefold. First, the hydration free energy per monomer is found to be strongly dependent on temperature and does not follow interfacial thermodynamics. Second, the temperature dependence profiles are distinct among the three hydrophobic polymers as a result of a hydrophobic size effect at the subnanometer scale. Third, the hydration free energy of a monomer on a macromolecule is different from a free monomer; corrections for the reduced hydration free energy due to hydrophobic interaction from neighboring units are required.
In the second example, we explore hydrophobicity in protein unfolding. Until now, the prevailing theory has been that hydrophobic surfaces unfold protein domains that adhere to them, by pulling out hydrophobic amino acids buried within the cores of the domains. We find that the tenth type 3 domain of the adhesion protein fibronectin ($FNIII_{10}$) retains significant structure at both hydrophobic and hydrophilic surfaces. Further, we find that the unfolding pathway is different from that observed in solution, and that the resistance to unfolding is usually divided into sequential events in each of two beta sheet units. Apparently unfolding is usually terminated at the beta strand ends. The forced unfolding measurement tends to disrupt beta-sheet elements from one end of the polypeptide to the other. Our results demonstrate how proteins can resist denaturation at surfaces, which suggests ways to engineer proteins that resist denaturation in applications such as biosensing.

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