The Hydrophobic Solvation Energies of Molecular-Scale Cavities Depend on the Detailed Structure of the Molecular Surface[1] ROBERT HARRIS, B. MONTGOMERY PETTITT, University of Texas Medical Branch — Both the energy (ΔG_{vdw}) of inserting an uncharged molecular cavity into solution by turning on the Lennard-Jones interactions between the solute and solvent and the energy (ΔG_{rep}) of inserting a nearly hard cavity into solution have often been assumed to increase linearly with the solvent-accessible surface area (A), in analogy with the energy of forming macroscopic cavities in solution. Because these energies are assumed to increase with A, they have often been assumed to drive protein collapse during folding. However we have shown that for molecular-scale cavities neither of these energies are simple linear functions of A. Additionally, for both alanine and glycine peptides we have shown that ΔG_{vdw} decreases with A, implying that ΔG_{vdw} opposes folding for these systems. We also show that assuming that ΔG_{rep} is linear in A for large molecules but linear in the solvent-accessible volume (V) for small molecules is inconsistent with our findings. Any theory that can accurately predict ΔG_{vdw} or ΔG_{rep} will have to consider the details of the molecular shape rather than relying on coarse measures, such as A and V.

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