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Desolvation effects and topology-dependent protein folding AL-LISON FERGUSON, ZHIRONG LIU, HUE SUN CHAN, Dept. of Biochemistry, Faculty of Medicine, University of Toronto — As a protein folds, water molecules must be excluded from the hydrophobic core, and thus desolvation barriers between the protein's constituents must be crossed in order to reach the final folded state. Previous research on continuum $G\bar{o}$ -like protein models has demonstrated that pairwise-additive desolvation potentials lead to more thermodynamically and kinetically cooperative folding/unfolding transitions (Z. Liu and H. S. Chan, *Phys. Biol.* **2**, S75-S85, 2005). The present work focuses on the role of this elementary desolvation potential in improving predictions of the well-known topology-folding rate relationship (K. W. Plaxco *et al*, *J. Mol. Biol.* **277**, 985-994, 1998) of small single-domain proteins. Recent computational studies without desolvation barriers have shown (S. Wallin and H. S. Chan, *J. Phys.: Condens. Matt.* **18**, S307-S328, 2006) that the observed correlation between topological parameters and folding rates is because these parameters may be proxies for rate-determining properties of the transition state, such as the activation free energy ΔG^\ddagger and activation conformational entropy ΔS^\ddagger . Including the desolvation barrier in the model results in stronger correlations between measures of topology and simulated folding rates / transition state properties, reinforcing the theory that even simple representations of the desolvation effect are important for understanding crucial features of protein folding.

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