Abstract Submitted
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Role of interfacial water in the binding of two proteins[1] JOSE CARO, KATHLEEN VALENTINE, JOSH WAND, Univ of Pennsylvania — Molecular recognition by proteins is fundamental to biology. Specific contacts at the interface (ΔH) and the release of solvating water ($T\Delta S_{solv}$) are often assumed to govern binding energetics. Typically, $T\Delta S_{solv}$ is obtained by calculating the surface area that becomes buried on binding, and by assuming a generic contribution from the hydrophobic effect. For some protein complexes, however, crystal structures display a large number of water molecules at the binding interface. This is the case for barnase-barstar, a protein-protein complex with over a dozen waters buried at the interface. Based on the entropy of fusion of water, this represents a very large energetic penalty. Yet, the complex forms with femtomolar affinity (ΔG_{bind} ˜80 kJ/mol). Interestingly, 9 of the buried waters are also observed in the crystal structure of unbound barnase. To evaluate the role of specific hydration in barnase-barstar, we used nuclear Overhauser (NOE) NMR methods to detect magnetization transfer between amide protons and water. The NOEs detected for both the free and bound states of barnase are consistent with the crystallographic waters observed. Order parameters of side chains directly hydrogen bonded to the rigid waters are also consistent with a pre-organized interface. NOE experiments performed in the confined, water-depleted space of a reverse micelle enabled detection of binding-induced changes in protein-water interactions far from the interface.

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