Hydration fingerprint in DNA recognition

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The molecular code of specific DNA recognition by proteins as a paradigm in molecular biology remains an unsolved puzzle primarily because of the subtle interplay between direct protein-DNA interaction and the indirect contribution from water and ions. Conversion of the non-specific, low affinity complex to a specific, high-affinity one is accompanied by the release of interfacial water molecules, the structure of which was hypothesized to govern target site location. To probe this tenet, the structure and energetics of water at the protein-DNA interface of the non-cognate BamHI complex was investigated by Grand Canonical Monte Carlo simulations and Proximity analysis. We also compared interfacial water properties of a damaged DNA containing a GU mismatch to the corresponding canonical sequence. Both studies demonstrate that water distribution as well as the interaction energies vary in a sequence specific manner. Thus we propose that interfacial waters can serve as a "hydration fingerprint" of a given DNA site by controlling complex-formation via local entropy contributions to the binding free energy.