23.3. PROTEIN–LIGAND INTERACTIONS

23.3.5.2. Short hydrogen bonds

The ultra high resolution refined structure of the PBP–phosphate complex is the first to show structurally the formation of an extremely short hydrogen bond (2.432 Å) between the Asp56 carboxylate of PBP and phosphate. Although this short hydrogen bond is within the proposed range of low-barrier hydrogen bonds with estimated energies of 12–24 kcal mol\(^{-1}\) (Hibbert & Emsley, 1990), its contribution to phosphate binding affinity has been assessed to be no better than that of a normal hydrogen bond (Wang et al., 1997). Thus, a unique role for short hydrogen bonds in biological systems, such as in enzyme catalysis (Gerlt & Gassman, 1993; Cleland & Kreevoy, 1994), remains controversial.

23.3.5.3. Non-complementary negative electrostatic surface potential of protein sites specific for anions

The presence of an uncompensated negatively charged Asp56 is unusual for an anion-binding site, as observed in PBP. In fact, a related discovery of profound ramification is that the binding-cleft region of PBP has an intense negative electrostatic surface potential (Fig. 23.3.5.3a) (Ledvina et al., 1996). Non-complementarity between the surface potential of a binding region and an anion ligand is not unique to PBP. We have reported similar findings for SBP, a DNA-binding protein, and, even more dramatically, for the redox protein flavodoxin (Fig. 23.3.5.3b) (Ledvina et al., 1996). Evidently, for proteins such as these, which rely on hydrogen-bonding interactions with only uncharged polar residues for anion binding and electrostatic balance, a non-complementary surface potential is not a barrier to binding. This conclusion is supported by very recent fast kinetic studies of binding of phosphate to PBP and the effect of ionic strength on binding (Ledvina et al., 1998).

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References