

S003 Calorimetry as a tool for understanding biomolecular interactions and an aid to drug design

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The binding of two biomolecules viewed from the atomic level is highly complex. It involves the formation, or removal of many individual non-covalent bonds both between the interacting molecules as well as with solvent. Currently our understanding of the quantification of this on the thermodynamic level is somewhat naïve.

Isothermal titration calorimetry (ITC) provides a rapid route to a full thermodynamic characterization of a biomolecular interaction. Direct determination of the change in enthalpy (ΔH) for complex formation and the use of this to probe the extent of an interaction throughout a titration enables the calculation of the equilibrium binding constant (K_B). With these terms a full thermodynamic characterisation of the interaction can be determined via the relationship; $-RT \ln K_B = \Delta G = \Delta H - T\Delta S$. Where R is the gas constant, T is the absolute temperature, ΔG and ΔS are the change in free energy and entropy respectively on going from free (unbound) to associated (bound) states.

Armed with these data what are we really able to understand about complex formation and can any of this information provide a useful tool to aid drug development? We have explored correlations between thermodynamic data and structural detail and are able to suggest ways in which these can be used to understand protein-ligand interactions.