

Structure, Free Energy, Enthalpy and Entropy in Protein-Ligand Interactions: A Database Approach

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Abstract:

Interactions of proteins with small molecules are central to many biological processes. Developing a detailed understanding of protein-ligand interactions is therefore fundamental to the molecular life sciences. An understanding of how structural perturbations correlate with the thermodynamics of binding forms a cornerstone of biophysical investigation.

To investigate how structure relates to the thermodynamics of binding, we have created a database of experimental data on protein-ligand interactions that have been characterized by both structural and calorimetric methods (<http://www.biochem.ucl.ac.uk/scorpio/scorpio.html>). The structures were analyzed in terms of buried apolar- and polar- surface area. These structural parameters were then correlated to the Gibb's free energy-, the enthalpy-, and entropy- of binding.

Contrary to common belief we find that there is no general relationship between the apolar surface area buried in forming a protein-ligand complex and the entropy. However, there is a significant correlation between the buried apolar surface area and the Gibb's free energy ($r^2=0.64$). Furthermore, we find that the buried polar surface area remains relatively constant for ligands of a wide range of sizes. The findings are discussed in terms of the evolution of selectivity and affinity in binding sites.