

Understanding molecular recognition processes using thermodynamic profiling and structural data

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The laws governing molecular recognition between molecules are interesting areas of study in modern chemistry. Why is it that some molecules form strong complexes? Is it that they prefer to exist in a complex? Change in Gibbs free energy (ΔG) determines this phenomenon. If complex formation leads to reducing free energy, it is spontaneous.

Free energy has two major contributions; it is enthalpic (ΔH) and entropic ($-T\Delta S$). Enthalpic changes depend on forming and breaking interactions between receptors, ligands, and water molecules. When complex hydrogen bonds are formed, van der Waals interactions are broken between receptor and solvent and ligand and solvent. Simultaneously, new interactions form between receptor and ligand: the solvent structure reorganizes on the receptor surface, intramolecular hydrogen bonds and other interactions change in the receptor, and the binding pocket undergoes conformational changes. In contrast, entropy depends on the amount water molecules the binding pocket releases and the receptor and ligand losing rotational and oscillating degrees of freedom. Both of these can be codependent.

As many factors affect energy, predicting the strength of ligand-receptor complexes can be difficult. This project is based on studying a series of congeneric compounds for the rational design of ligands, while considering the effects mentioned above. The project is aimed at determining the relationship between the physicochemical properties and structural and/or electrostatic particles, and the energy effect caused by forming the complex.

