COSMO Polarization Charge Densities as Good Descriptors for the Quantification of Hydrogen Bond Enthalpy and Free Energy in Solution

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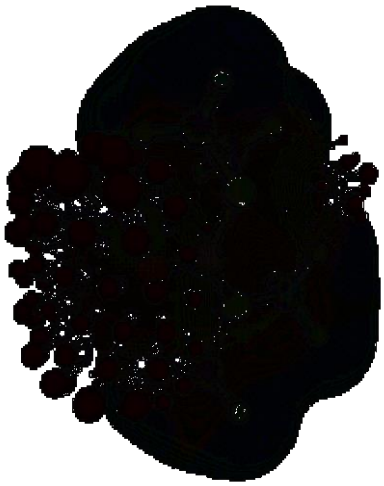
The concept of hydrogen bonding is extremely important for the understanding of many phenomena in liquid systems and for almost all biochemical phenomena. Despite of its fundamental importance, our knowledge about hydrogen bonding and the available schemes for the quantification of hydrogen bond enthalpy and entropy are surprisingly limited. This is due to the complex nature of hydrogen bonding, since it arises from a complicated combination of electrostatic attraction, molecular orbital interactions, dispersion and Pauli repulsion. For small hydrogen bonded dimers in vacuum complete basis set extrapolated coupled cluster calculations seem to provide reliable results [1], but a fully theoretical description of hydrogen bonding for molecules of practical relevance in solution is currently far out of reach.

Without claiming to have found a theoretically fundamental explanation of hydrogen bonding, we have demonstrated in a series of large scale studies [2,3] that hydrogen bond enthalpy appears to be proportional to the product of the COSMO polarization charge densities [4] of donor and acceptor. Based on experimental hydrogen bond enthalpies reported by Le Questel *et al.* [5], we also succeeded in finding a consistent expression for hydrogen bond entropy. Since COSMO polarization charge densities are computationally easily available, this allows for the predictive quantification of the hydrogen bond strength of almost any combination of donors and acceptors at variable temperature. Our findings led to improvements of the hydrogen bond expression in the COSMO-RS solvation model [6,7], but also allow for more refined hydrogen bond expressions in force-fields.



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