MS043.O06

Topological analysis of hydrogen bonds and interaction energies in proteins

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Structure of a protein relates to its function and it is well understood that during the folding process, the nonpolar side chains get buried due to hydrophobic effects and the main-chains form N-H•••O=C hydrogen bonds. Experimental and theoretical evidences [1] claim that the electrostatic energy term of hydrogen bonding energy predominates during the folding to stabilize protein. The major hydrogen bonding in globular protein occurs between the main-chain N-H and C=O groups, which are the key building blocks of both α-helix and β-sheet structures. Knowledge of such hydrogen bonding networks and the local electrostatics in proteins is essential for proper thermodynamic modeling, prediction of protein folding pathways and binding interactions. Research in the area of protein charge density analysis has recently been stimulated particularly with the interest in the topological analysis of hydrogen bonds, protein-ligand interactions and their electrostatics.[2] Such analyses are performed based on electron density database transfer approach, thanks to ELMAM-2 database. Many more such studies on variety of protein systems might allow researchers to understand the properties of hydrogen bonds better and help characterizing them as done so in small molecule systems. In this line, based on ELMAM-2 database we have modelled charge densities of several high-resolution X-ray protein structures as deposited in the Protein Data Bank. In this presentation we will discuss the topological properties of N-H•••O=C hydrogen bonds present both in the α-helices and β-sheets and estimate their electrostatic interaction energies. Further, efforts will be made to provide a qualitative and quantitative picture of protein-ligand interactions from Hirshfeld surface approach and quantum kernel energy method,[3] respectively and correlate the findings with those obtained from charge density analysis approach.

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Keywords: Hydrogen bonding, Topological analysis, Kernel Energy Method