24. Allosteric regulation, the role of the unprotected hydrogen bonds

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At present, the complex mechanisms that govern protein interactions and enzymatic regulation remain poorly understood. In this work, using computational analysis of protein coordinates obtained from the Protein Data Bank, we found evidences that such kind of problematic could be resolved taking into consideration three bodies interactions, two bodies for protein backbone hydrogen bonds (HB) and the third body for carbonaceous (carbon atoms in residues not bonded to N, O, P, S) around this HB. In the particular case of 3-phosphoinositide dependent protein kinase-1 (PDK1), the ability of ligands to shield or "wrap" dehydrons (HBs not sufficiently protected from water by carbonaceous) in the allosteric domain of the enzime was analyzed. The ligands induce morphological changes in the enzime, so we followed the variations in the dehydron pattern in the catalytic domain of the enzyme to justify its activity. The results obtained from this theoretical approach could help in the understanding of the relationship between the enzime structure and action of drugs (the keystone in drug design) and the way in which enzymes operates.