Explore Hydrogen-bond Cooperativity in Intact Protein

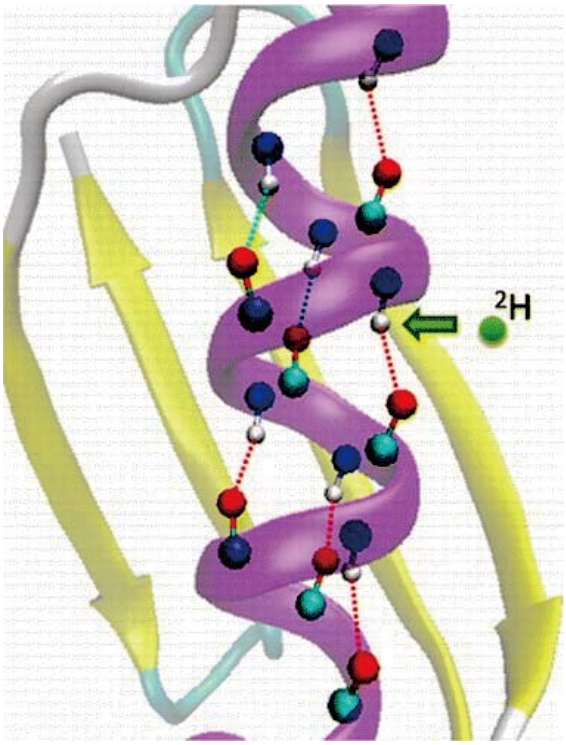
Human diseases may be caused by the malfunction of an intact protein. Hydrogen bond (h-bond) is one of the key interactions in maintaining the structure of a protein and facilitating its function. The presence and extent of h-bond cooperativity in proteins remains a fundamental question, and quantitative analysis of h-bond cooperativity is still lacking.

The Modeling and Simulation Group from the Qingdao Institute of Bioenergy and Bioprocess Technology of the Chinese Academy Sciences, led by YAO Lishan, has recently demonstrated a quantitative analysis of the h-bond cooperativity in a intact (or natural) protein.

Their study was conducted through a modified hydrogen/deuterium (i.e. H/D) exchange NMR (Nuclear Magnetic Resonance) spectroscopy method. The method is based on the fact that the substitution of NH by ND in a backbone amide group slightly weakens the N−H•••O−C h-bond. Such a substitution impacts the h-bonds nearby as reflected by their ^{1}H and ^{15}N chemical shift changes of the NMR spectra. The fitting of the chemical shifts of the nearby residues to the exchange rates provides new quantitative insights into the cooperativity of h-bonds in the protein.

Experimental results showed that the H/D exchange at amide sites $i-3$ to $i+3$ all perturbs the h-bond at amide site i of α-helix, suggesting a positive cooperativity between these 6 h-bonds and the h-bond at amide site i. The quantum mechanical (QM) calculations demonstrated that the cooperativity is originated from the electrostatic polarization which affects the peptide plane electric dipole moment and thus the h-bond strength. The experimental and theoretical results implied very good consistence.

This work is the first to detect the h-bond cooperativity in an intact protein α helix. The approach can also be employed to study h-bond cooperativity in β-sheets (another important structure unit within a protein, besides α helix) of a protein or other biomolecules such as DNA and RNA. Such studies may lead to fundamental understandings of the question for practical or diagnostic applications in future.



Perturbation of a backbone hydrogen bond creates a response of nearby hydrogen bonds.

Their paper has been published in the *Journal of the American Chemical Society*.