Biomacromolecules at work: watching the details by solution NMR methods

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High resolution NMR is one of the most versatile tools for the quantitative study of biomolecular interactions at atomic resolution. Traditionally, NOEs and chemical shift perturbation methods are used to determine molecular geometries and to identify contact surfaces, but more recently weak alignment, anisotropic diffusion and scalar couplings across hydrogen bonds (H-bonds) provide additional information.

We will give examples of such technologies applied to the function of several biomacromolecules. In particular, we could recently follow the structural, kinetic, and thermodynamic details of the activation of the cellular adhesion protein cadherin by propeptide processing (1), of the TipA multidrug resistance protein upon antibiotic binding (2), of the trimerization and folding of foldon, a small and very efficient trimerization domain of the T4 phagehead (3, 4), and of disulfide formation in minicollagens, which are the major constituents of the extremely pressure resistant nematocyst outer wall (5).

By their strong dependence on the overlap of donor and acceptor electron wavefunctions, scalar couplings across H-bonds (6), present a unique tool to monitor changes in macromolecular H-bond geometries, when biomacromolecules are subjected to different conditions. We have extensively explored the use of $^{h3}J_{NC'}$ couplings across N-H···O=C H-bonds in proteins (7) and of $^{h2}J_{NN}$ couplings across N-H···N H-bonds in nucleic acids (8) to follow ligand binding (9), folding (10), thermal denaturation (11), and H/D isotope effects (12). More recently, not only N-H···O=C H-bonds, but also the enigmatic C^{a}-H^{a}···O=C hydrogen bonds could be detected directly via $^{h3}J_{CaC'}$ couplings (13).

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