NMR spectroscopy of biomolecular interactions

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The introduction of isotopic enrichment of macromolecules with ^{13}C and ^{15}N and the advent of multidimensional, heteronuclear techniques has increased the molecular weight limit for studies by high resolution NMR into the 50-100 kDa range. Besides providing structural and dynamical information, NMR is a unique tool for the study of biomolecular interactions in solution. The studied interactions traditionally comprise ligand binding, macromolecular aggregation, and solvent interactions, but more recently also hydrogen bonds (H-bonds).

In the first part, we will show results on the spectroscopy of individual H-bonds. The study of such interactions has been made possible by the discovery of electron-mediated, scalar couplings across H-bonds in RNA, DNA, proteins, and their complexes. These scalar couplings give evidence for the correlated motion of electrons on both sides of the hydrogen bridge. As a practical application, they can be used to identify all three H-bond partners, i.e. the donor, the acceptor and the proton from a single COSY experiment. The size of the trans-hydrogen bond scalar couplings is a sensitive function of the donor-acceptor distance. Therefore, the couplings are a precise monitor of the H-bond geometry. We will describe applications to a number of different folded and unfolded biomacromolecules and discuss the possibility to obtain insights into macromolecular stability and macromolecular interactions from the exact quantitation of the H-bond couplings.

In the second part, we will show results on the NMR determination of structure and interactions of several macromolecular complexes. NMR spectroscopy is one of the few methods yielding information on weak molecular interactions. Classically, contact surfaces for such interactions can be derived by chemical shift perturbations. However, more recently the information from weak anisotropic alignment forces and from anisotropic diffusion can be used to orient reaction partners relative to each other. We will give examples for protein complexes involved in cell-cell adhesion and multidrug resistance.

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