Towards Quantum Chemical NMR Chemical Shifts of Proteins 2: Level of Theory, Basis Set, and Solvents Model Dependence

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Calculations of accurate NMR chemical shifts of proteins, protein-protein and protein-ligand complexes are highly valuable in many applications like NMR structure evaluation and complex-structure predictions. We will present calculations using our fragment-based quantum chemical method: the adjustable density matrix assembler (ADMA) [1, 2]. In such calculations the target system is subdivided into small fragments, for which separate quantum chemical calculations are performed and which are then combined to get an approximation of the macromolecule.

A systematic investigation was performed in which the influence of the theory, the basis set size, the inclusion or exclusion of an implicit solvent model, and partial charges were used for the description of additional parts of the macromolecule [3]. The results of ^{13}C chemical shifts are in good agreement with the experiment. An even better agreement with the experiment is observed in the calculation of the 1H chemical shifts, when polar protons are not taken into account. The polar protons and ^{15}N chemical shifts deviate more strongly from experiment due to the insufficient treatment of solvent effects and conformational averaging. Approaches to overcome these limitations will be outlined.

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3. Frank A., Onila I., Möller H. M., Exner T. E., *Proteins*, **2011,** *79*, 2189-2202