Linear-Scaling *ab intio* NMR Chemical Shifts Calculations for Proteins Based on Automated Fragmentation QM/MM Approach

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Abstract

An automated fragmentation quantum mechanics/ molecular mechanics approach (AF-QM/MM) has been developed to routinely calculate the *ab initio* NMR chemical shielding constants for proteins. The AF-QM/MM method is truly linear-scaling and trivially parallel. A general fragmentation scheme is employed to generate each residue-centered region which is treated by quantum mechanics, and the environmental electrostatic field is described with molecular mechanics. The AF-QM/MM method shows a good agreement with the full system calculations for the NMR chemical shieldings as tested on the Trp-cage. The RMSEs for ^{1}H, ^{13}C and ^{15}N NMR chemical shieldings are equal or less than 0.09ppm, 0.32ppm, and 0.78ppm, respectively for all the HF and DFT calculations in this work. Among the charge models used, AMBER, AM1/CM2, PM3/CM1, PM3/CM2 give good representations of the electrostatic field for AF-QM/MM NMR chemical shielding calculations. The correlations between experimental ^{1}H NMR chemical shifts and theoretical predictions are over 0.95 for AF-QM/MM calculations using B3LYP with 6-31G**, 6-311G** and 6-311++G** basis sets. Our study also demonstrates that the conformational change of protein structures plays an important role in the accurate prediction of NMR chemical shifts.