

CHARMM force field parameters for simulation of reactive intermediates in native and thio-substituted ribozymes

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Abstract

Force field parameters specifically optimized for residues important in the study of RNA catalysis are derived from density-functional calculations in a fashion consistent with the CHARMM27 all-atom empirical force field. Parameters are presented for residues that model reactive RNA intermediates and transition state analogs, thio-substituted phosphates and phosphoranes, and bound Mg^{2+} and di-metal bridge complexes. Target data was generated via density-functional calculations at the B3LYP/6–311++G(3df,2p)//B3LYP/6–31++G(d,p) level. Partial atomic charges were initially derived from the CHelpG electrostatic potential fitting and subsequently adjusted to be consistent with the CHARMM27 charges and Lennard-Jones parameters were determined to reproduce interaction energies with water molecules. Bond, angle and torsion parameters were derived from the density-functional calculations and renormalized to maintain compatibility with the existing CHARMM27 parameters for standard residues. The extension of the CHARMM27 force field parameters for the non-standard biological residues presented here will have considerable use in simulations of ribozymes, including the study of freeze-trapped catalytic intermediates, metal ion binding and occupation, and thio effects.

Keywords

molecular dynamics, RNA, metal ions, thio effects, phosphorane