Point Charges Meet Accuracy of Multipoles: Presenting Atom-Centered Lebedev Charged Spheres

Maxim V. Ivanov and Qadir K. Timerghazin

Department of Chemistry, Marquette University, Milwaukee, Wisconsin

Atom-centered point charge model of the molecular electrostatics remains a major workhorse in the atomistic biomolecular simulations. However, this approximation fails to reproduce anisotropic features of the molecular electrostatic potential such as lone pairs, σ-holes and π-systems and the methods of charge-fitting are often associated with numerical instabilities. In this contribution we provide an in-depth analysis of these limitations and offer a novel approach to describe electrostatic interactions.

By analyzing the charge fitting problem from first principles, as an example of the inverse problem, we show that the inaccuracy of the atom-centered point charges and numerical instabilities of the charge-fitting problem are intrinsic to the problem. Atom-centered point charge model can be viewed as an irregular numerical quadrature that does not integrate spherical harmonics, except for the first two terms, and thus cannot reproduce high order multipoles. This insight suggests that if the point charges are arranged using the quadrature that exactly integrates spherical harmonics, e.g. Lebedev spherical grid, the resulting point charge model can exactly reproduce multipoles up to a given rank. Furthermore, by placing the charged Lebedev spheres at the atomic nuclei we extend the traditional atom-centered point charge approximation to include high order atomic multipoles within the point charge approximation. As a result, multipole-multipole interactions can be calculated as a pairwise Coulombic interaction between the off-center point charges instead of direct computation of the multipole-multipole terms. Existing support of the off-center point charges through the virtual sites, i.e massless particles, in simulation packages such as AMBER, GROMACS, OpenMM allows an immediate implementation of this model to achieve multipolar quality of the force field within the point charge framework.

In this contribution we present mathematical origin and numerical validation of the proposed model as well as our recent results on its implementation in AMBER package.

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