JCTC Journal of Chemical Theory and Computation

Special Issue on Polarization

Computer simulations of organic and biomolecular systems consisting of thousands of explicitly represented atoms began in earnest in the 1970s. Molecular dynamics or Monte Carlo statistical mechanics were used to model, for example, liquid water, aqueous solutions of simple molecules and ions, organic liquids, and small proteins in vacuum. A key aspect of the work was the representation of the intra- and intermolecular energetics. In view of the size of the systems and available computer resources, the usual choice was classical force fields that had roots in 'molecular mechanics' studies of organic molecules going back to the 1950s. The simulation community was unified on this point, and the general force fields such as AMBER, CHARMM, and OPLS, which arose during the 1980s, adopted nearly identical functional forms. This included the representation of molecules as collections of atom-centered interaction sites with fixed partial charges. The electrostatic energy is then simply determined by the Coulombic interactions between the charged sites. Since the charges are fixed, there is no explicit treatment of electronic polarization, and intermolecular interactions are treated as pairwise additive. Though the impact of this approximation is diminished through the use of effective pair potentials with enhanced charges, the lack of explicit polarization is physically incorrect and is well-known to be problematic for interactions with charge concentrated ions, interactions of ions with π-electron systems, and even for less obvious cases such as polar solutes in low-dielectric media.

Consequently, there has been steady interest since the 1970s in the development and use of polarizable force fields with early work focusing on liquid water and ions in water. Nevertheless, after 30 years and universal agreement on the importance of the problem, generally accepted, broadly applicable polarizable force fields have not emerged, multiple treatments of polarizability (inducible dipoles, fluctuating charges, Drude oscillators, etc.) remain under consideration, and simulations of biomolecular systems with polarizable force fields are still uncommon. Though there is no denying that development and thorough testing of a polarizable force field are a large undertaking, overall, research in the area has taken a back seat to myriad applications of nonpolarizable force fields in modeling ever larger and more complex systems on longer timescales. Though the latter work allows contact with ongoing experiments in molecular biology, medicinal chemistry, and materials science, the impact and prospective capabilities of the simulation work are affected by the quality of the underlying description of molecular energetics. Quantum mechanical treatment of large systems and ab initio molecular dynamics have also advanced during this period and directly incorporate polarization effects; however, they do not provide a general solution as there will always be a class of problems for which use of more rigorous methods is not practical.

In this atmosphere, it was decided to have an issue of the *Journal of Chemical Theory and Computation* with a focus on current research on polarizability and polarizable force fields. Twenty-one articles are included that reflect the state-of-the-art and new developments. They provide a valuable platform for future advances on this important topic.

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