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REVIEW ARTICLE

Poisson-Boltzmann Solvents in Molecular Dynamics Simulations

Jun Wang, Chunhu Tan, Yu-Hong Tan, Qiang Lu and Ray Luo*

Department of Molecular Biology and Biochemistry University of California, Irvine, CA 92697-3900, USA.

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Abstract. Recent years have witnessed significant improvement in implicit solvents based on the Poisson-Boltzmann theory, whether in the forms of numerical solution or analytical approximation. Especially worth noting are the improvements and revisions of those implicit solvents for stable dynamics simulations. Given these technical advancements, attentions are now paid to the quality of implicit solvents as compared with the more expensive explicit solvents. The new developments in nonpolar solvents mentioned above and reviewed elsewhere will also result in more accurate simulations of biomolecules. We have also touched the new challenges facing the implicit solvents. That is how to incorporate these solvents in the emerging polarizable force fields. New challenges could also arise from the assumptions underlying all implicit solvents, as recently explored to couple electrostatic and nonelectrostatic components together. In addition, hybrid solvents could eventually become a reality for dynamics simulation even this has been proposed in the early days of computational biochemistry. It is likely that such hybrid solvents will offer the necessary accuracy, as they no longer average out the very degrees of freedom that are of interest in studies where solute/solvent coupling is crucial.

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Contents

*Corresponding author. *Email addresses:* wjun78@gmail.com (J. Wang), chunhutan@hotmail.com (C. Tan), yuhongt@uci.edu (Y.-H. Tan), qianglu@gmail.com (Q. Lu), rluo@uci.edu (R. Luo)

1 Introduction

Molecular dynamic (MD) simulation is one of the important theoretical methods to investigate the structures, dynamics and kinetics of proteins at the atomic level. To describe the interactions between atoms, MD simulations usually adopt a relatively simple potential energy function (U), as follows

$$U=\sum_{\text{bonds}} k_b(b-b_0)^2+\sum_{\text{angles}} k_\theta(\theta-\theta_0)^2+\sum_{\text{torsions}} k_\phi[\cos(n\varphi+\delta)+1] + \sum_{\substack{\text{atom}\\ \text{pairs}}}\left[\frac{Q_iQ_j}{r_{ij}}+\frac{A_{ij}}{r_{ij}^{12}}-\frac{B_{ij}}{r_{ij}^{6}}\right]. \tag{1.1}$$

The first three summations are over deviations of bonds (b) from their equilibrium values (b_0), deviations of angles (θ) from their equilibrium values (θ_0), and rotatable bonds (torsion angles φ with phase n and offset δ). The final summation is over pairs of atoms i and j with charges Q_i and Q_j separated by distance r_{ij}. It describes electrostatic interactions that are represented by a Coulombic potential, and dispersion and exchange repulsion interactions that are represented by a Lennard-Jones 6-12 potential. The parameters in Eq. (1.1) along with the function form of Eq.(1.1) are called force field. Many force fields have been developed for biomolecular simulations, such as Amber [1–6], CHARMM [7,8], and OPLS [9–11]. Use of the potential energy function in Eq. (1.1) allows a rather efficient numerical procedure to be developed to solve the Newtonian equation of motion

$$\frac{d^2\mathbf{r}}{dt^2}=-\nabla U. \tag{1.2}$$

The overwhelming adoption of molecular dynamics in molecular biophysics can be contributed to the often stringent requirement that an atomic-detailed description of biomolecules must be used to elucidate their structures and functions. However even with such a simple functional form of Eq. (1.1), many fundamental biomolecular processes remain largely inaccessible to molecular dynamics simulations when relevant timescales reach microseconds and system sizes exceed more than a few hundred residues. The computational inaccessibility partially comes from the requirement for an accurate description of the aqueous environment that is essential for atomistic biomolecular simulations. To fulfill the requirement even for a medium-sized biomolecule requires thousands of discrete water molecules to be placed around it. The computational cost for