

Image Charge Methods for a Three-Dielectric-Layer Hybrid Solvation Model of Biomolecules

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Abstract. This paper introduces a three dielectric layer hybrid solvation model for treating electrostatic interactions of biomolecules in solvents using the Poisson-Boltzmann equation. In this model, an interior spherical cavity will contain the solute and some explicit solvent molecules, and an intermediate buffer layer and an exterior layer contain the bulk solvent. A special dielectric permittivity profile is used to achieve a continuous dielectric transition from the interior cavity to the exterior layer. The selection of this special profile using a harmonic interpolation allows an analytical solution of the model by generalizing the classical Kirkwood series expansion. Discrete image charges are used to speed up calculations for the electrostatic potential within the interior and buffer layer regions. Semi-analytical and least squares methods are used to construct an accurate discrete image approximation for the reaction field due to solvent with or without salt effects. In particular, the image charges obtained by the least squares method provide accurate approximations to the reaction field independent of the ionic concentration of the solvent. Numerical results are presented to validate the accuracy and effectiveness of the image charge methods.

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1 Introduction

The study of electrostatic interactions using macroscopic continuum models [5, 11, 17, 26, 40] has been widely conducted for investigating structure, function, and properties of protein molecules in an aqueous environment. These implicit models characterize the solvent in terms of macroscopic physical quantities such as dielectric constants and Debye lengths, and thus greatly reduce the degrees of freedom in comparison with explicit atomistic solvent models. In macroscopic models, the solute molecule is usually considered as a uniform low-dielectric medium (with a dielectric constant between one and four) with a fixed charge distribution, and the solvent is treated as a homogeneous medium with a high dielectric constant, such as 80 for water. A Linearized Poisson-Boltzmann (LPB) equation is then solved to obtain the electrostatic potential of the system.

Historically, Born [8] first studied the solvation effects for an ion placed at the center of a spherical region with a low dielectric constant embedded in a high-dielectric medium, and derived the electrostatic free energy. Onsager [32] extended this study to a dipole. Both Born and Onsager models are special cases of the results of Kirkwood [25] and Tanford and Kirkwood [38], which represented the solute molecule as a collection of fixed charges within a spherical cavity. The LPB equation was solved analytically for spherical geometries in these early studies. More recent work has considered ellipsoids [4, 13]. For an irregular boundary, numerical methods [6, 24, 28] such as finite difference and finite element methods in three-dimensional grids must be used. However, numerically solving the LPB equation is computationally expensive. To analytically treat biomolecules with general geometries, the hybrid implicit/explicit model using a spherical cavity has been developed [7, 31]. In addition to the biomolecule solute, such as a protein, the spherical cavity contains several layers of explicit water molecules to model the interactions between the solute and solvent molecules.

In previous work, we developed a multiple image charge approximation [9] to the Kirkwood series solution using numerical quadratures of the line image charge representation [18, 27, 29, 30] of the reaction field from pure water. The locations of resulting image charges are related to Gauss quadrature points. Although less accurate, a single image charge [19] and its improved version [1] have been widely applied in molecular dynamic and Monte Carlo simulations [21, 33, 41]. Employing more images improves the approximation of the Kirkwood solution, especially closer to the boundary. The method of multiple discrete images has also been extended to treat the reaction field for ionic solvents [14, 15, 43] in the case of low ionic strength.

Unfortunately, continuum solvation models with piecewise constant dielectric functions produce unphysical reaction fields within the spherical cavity near the boundary. This artifact strongly affects the charged solvent molecules (i.e. water) near the boundary. Inaccurate estimation of the pairwise electrostatic interaction [35] results because of improper electrostatic screening by the high-dielectric solvent. To overcome this drawback, pairwise electrostatic interactions near the interface have been modeled using a distance-