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Accuracy and efficiency in computing electrostatic potential for an ion channel model in layered dielectric/electrolyte media

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ABSTRACT

This paper will investigate the numerical accuracy and efficiency in computing the electrostatic potential for a finite-height cylinder, used in an explicit/implicit hybrid solvation model for ion channel and embedded in a layered dielectric/electrolyte medium representing a biological membrane and ionic solvents. A charge locating inside the cylinder cavity, where ion channel proteins and ions are given explicit atomistic representations, will be influenced by the polarization field of the surrounding implicit dielectric/electrolyte medium. Two numerical techniques, a specially designed boundary integral equation method and an image charge method, will be investigated and compared in terms of accuracy and efficiency for computing the electrostatic potential. The boundary integral equation method based on the three-dimensional layered Green's functions provides a highly accurate solution suitable for producing a benchmark reference solution, while the image charge method is found to give reasonable accuracy and highly efficient and viable to use the fast multipole method for interactions of a large number of charges in the atomistic region of the hybrid solvation model.

1. Introduction

Ion channels play a key role in many biological processes, including cell–cell communication, signaling, muscle contraction, etc. And it is well known that the electrostatic interaction is important in the selectivity and transport of ions through biological ion channels. The description of the membrane/solvents around an ion channel can be either atomistic as in an explicit model or continuum as in an implicit model. The selection of a specific model for the solvent depends on the accuracy and efficiency desired for the overall simulation. In order to take advantage of the accuracy of the explicit model and the efficiency of the implicit model, the explicit/implicit hybrid solvation model has been actively studied [1–7]. In such a model, the simulation system is partitioned into two regions, the inner region, usually of a regular geometric shape such as a finite cylinder in this study, containing passing ions and transmembrane channel proteins, and the remaining outer region exterior to the cylinder. In the former region, an atomistic description is used for the ion channel proteins and transgressing ions, while in the latter region, the membrane and solvents are described by dielectric constants or Debye–Hückel length parameters modeling the solvents' conductivity and concentrations. In molecular dynamics simulations using a hybrid solvation model, only the atoms inside the explicit region are dynamically simulated while the effect of the implicit region is included by the use of a reaction field, which results from the polarization of the implicit solvents and membrane by charges

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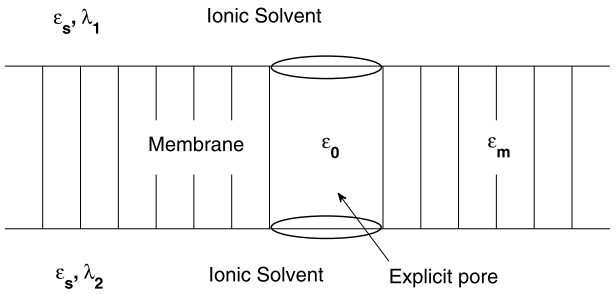

Fig. 1. Schematic illustration of an ion-channel hybrid model.

inside the explicit region. Therefore, for the hybrid solvation model of ion channels in our study it is critical to have a fast and accurate method to calculate the reaction field for a finite-height cylinder embedded in a layered dielectric/electrolyte medium for ion channel simulations in atomic details.

Due to the complicated and infinite inhomogeneous setting of the hybrid solvation model, it is a computational challenge to find an accurate and fast numerical method for the reaction field of the implicit region. Traditional finite difference or finite element methods have been used to solve the Poisson equation for the reaction field; however, issues such as artificial boundary conditions for the truncated computational domain and the interface treatment for the membrane and ion-channel walls have not been resolved completely. Previous work treating dielectric interfaces for ion channels includes computing the polarization surface charges using a variational formulation [15], empirical formulas for self-energies of ions in channels [16], and an asymptotical analytical method [17,18]. A more natural and accurate candidate for handling the infinite region and dielectric boundaries is to use a surface integral equation method applied to the boundary of the finite-height cylinder cavity while the interface conditions along the membrane/solvents are handled by a layered Green's function, which addresses the interface conditions in its definition. Alternatively, the image charge method, as a semi-analytical approach, can also be used to find the reaction field for regular shaped geometries including dielectric spheres [9] and a finite-height cylinder. These two methods will be the subjects of study in this paper.

One of the challenges for high accuracy in surface integral equation method comes from the difficulties caused by the corner/edge singularities of the surface. There have been a large number of special techniques proposed to eliminate the error pollution from the geometry irregularities, including graded meshes and special charge basis [11–14]. However, simply and easily implementable methods are still in demand. This paper will adopt a different approach to circumvent this difficulty for the hybrid solvation model of ion channel by deforming the geometry of the finite-height finite cylinder to a smooth semi-sphere top cylinder. Then, by using layered Green's functions for the layered media inside and outside the new extended geometry, we can remove the singularity effect arising from the geometric edges. The resulting surface integral equation method can be used as a universal benchmark method for validating other types of numerical solutions including the finite difference and finite element methods. With the specially formed surface integral equation method, we are also in a position to carefully study a previously proposed image charge method for finding the reaction field for the finite-height cylinder [23]. Comparison and validation of the image charge method will be conducted.

The rest of the paper is organized as follows. In Section 2, the background material on the hybrid solvation model for ion channels is given and how the reaction field can be used for molecular dynamics simulation of ion channels would be discussed. Section 3 presents the concept and construction of the layered Green's function for the Poisson and Poisson–Boltzmann equations. Section 4 formulates the surface integral equation method for the electrostatic potential based on an extended geometry for the finite-height cylinder. Section 5 reviews the previous image charge method. In Section 6, numerical tests with both the boundary integral equation method and the image charge method are carried out and compared. Finally, a conclusion is given in Section 7.

2. A hybrid solvation model for ion channels

The hybrid solvation model for ion channels in Fig. 1 consists of a cavity of a finite-height cylinder embedded in a layered dielectric/electrolyte medium representing the biological membrane and ionic solvents. Inside the cylinder, the channel proteins and transgressing ions are treated with explicit atomistic representations while, outside the cylinder, the membrane and solvents are treated as continuous dielectrics. Moreover, the ionic solvents above and below the membrane are modeled by the Debye–Hückel (D–H) mean-field theory for the mobile ion density distributions, which gives the Poisson–Boltzmann (P–B) equation for the electrostatic potential in the electrolyte solvents [19].

As shown in Fig. 1, the dielectric constants in the interior of the cylinder, the membrane, and the ionic solvent are denoted by ε_0, ε_s, and ε_m, respectively. And λ_1 and λ_2 are the inverse Debye–Hückel lengths of the ionic solvents above and below the membrane, respectively. Now, let us assume that point charges q_i locate at $\mathbf{r}_i$ inside the cylinder. The potential field ϕ satisfies the following P–B equation: