Image Approximations to Electrostatic Potentials in Layered Electrolytes/Dielectrics and an Ion-Channel Model

Huimin Lin\textsuperscript{a} Zhenli Xu\textsuperscript{b} Huazhong Tang\textsuperscript{a} Wei Cai\textsuperscript{c,d}

\textsuperscript{a} CAPT & LMAM, School of Mathematical Sciences, Peking University, Beijing 100871, China
\textsuperscript{b} Institute of Natural Sciences, and Department of Mathematics, Shanghai Jiao Tong University, Shanghai 200240, China
\textsuperscript{c} Department of Mathematics and Statistics, University of North Carolina at Charlotte, Charlotte, NC 28223, USA
\textsuperscript{d} Beijing International Center for Mathematical Research, Beijing, 100871, China

Suggested Running Head:
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Corresponding Author:
Prof. Wei Cai
Department of Mathematics and Statistics,
University of North Carolina at Charlotte,
Charlotte, NC 28223-0001
Phone: 704-687-4581, Fax: 704-687-6415,
Email: wcai@uncc.edu

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Abstract

Image charge approximations are developed for electric potentials in the Poisson-Boltzmann theory in inhomogeneous media consisting of dielectrics or electrolyte solutions such as the layered structure in a membrane or cylindrical ion-channels. The image charges are obtained either by a least square fitting between the potential of unknown images and the exact reaction potential (for the layered media or cylindrical region) or by a Prony fitting to the Fourier transform of the exact potential (layered media only) and a Sommerfeld-type identity, which yields the locations and strengths of the image charges. Next, combining the results for the two geometries, the image charge approximation for the reaction potential, due to a charge inside the ion-channel, is obtained, which accounts for the polarization of the region outside the ion-channel (consisting of a membrane and electrolyte solutions below and above). Such an approximation to the reaction field in the ion-channel model is the key component for an explicit/implicit hybrid treatment of electrostatics interaction in modeling ion-channels. Numerical tests show that the proposed method has attractive performance in computing electrostatic interactions of source charges inside the ion-channel via a simple summation of pairwise interactions among source and image charges.

Key words: Poisson-Boltzmann equation, layered electrolytes and dielectrics, method of images, ion channels, hybrid explicit/implicit solvent models
1. Introduction

The electrostatic force is one of the most important forces in the structure and stability of biomolecules in an aqueous environment [1,2]. The classical electrostatic theory applies to the medium comprised of solute macromolecules and surrounding solvent environment. The Poisson-Boltzmann (PB) theory [2–5] is based on a mean-field approximation [6], where the force on an ion resulting from the potential of the mean field is given by the ion charge times the macroscopic electrostatic potential of the solute-solvent system. The PB theory is successful in describing the electrostatic interaction of biological systems as long as the electrostatic coupling strength is weak, for instance, proteins or DNAs in the natural cellular environment [7] where the linearized PB approximation is often used to account for the influence of monovalent salt such as NaCl.

The description of solvents surrounding a solute or 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 simulation. In order to take advantage of the accuracy in the explicit model and the efficiency of the implicit model, hybrid explicit/implicit solvent models have been studied [8–14]. In such a model, the simulation system is partitioned into two regions. The inner region, usually of a regular geometric shape such as a sphere or a finite cylinder, containing the solute or the transmembrane channel under study, and a remaining region exterior to the sphere or the cylinder. In the former region, an atomistic description is used for the solute and the solvent molecules while in the latter region, the membrane/solvent is described by dielectric constants or Debye-Hückel length parameters, which reflect the salt concentration. In the molecular dynamic simulation within the hybrid 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 solvent by the charges inside the explicit region. Therefore, it is important to have a fast and accurate method to calculate the reaction field for a given geometry of the explicit region. In the case of a sphere, the classical Kirkwood series expansion [15,16] can be used to calculate the reaction field of point charges inside the spherical cavity. However, the Kirkwood expansion has a slow convergence rate, especially for charges close to the boundary of the cavity. The image charge methods [17–19] provide a simple alternative to calculate the reaction field efficiently. As the images are in Coulombic form, approximating the reaction field with discrete image charges will result in a linear scaling calculation once fast algorithms such as the fast multipole method [20–22] are utilized to speed up the particle interactions. Furthermore, the multiple image methods [22–24,13,25] have been developed to provide an approximation with high order accuracy by increasing the number of images. Similar results have been applied to a cylinder [26], which offers an efficient approximation to an exact series solution in terms of cylindrical harmonics [27], where image charges are obtained through an optimization process.

The main objective of this paper is to develop the method of image approximation to the reaction field of the solvent/membrane region surrounding an ion-channel model for the computer simulations of biological ion channels [28–30], which are of interest in many fields such as electrophysiology, cell biology and biomedical science [31,32]. In order to achieve this goal, we will find image approximation to electric potential in the presence of two types of material interfaces: the layered medium from membranes and a cylindrical region from the ion channel. Then, by combining the results of image approximation for the two types of interfaces, we will be able to derive the image charge approximation of the reaction field of the ion-channel model. In the hybrid model for the ion-channel simulations, the explicit region is usually chosen as a finite
cylindrical geometry, which includes the interested transmembrane proteins, some ions and waters, and a portion of membrane residues. Outside the finite height cylinder, the membrane and bulk solvent are treated implicitly as a continuum medium by the mean field approximation (refer to Fig. 5). Previously, for solvents of pure water, the image method was developed [26] to calculate the reaction field in the ion-channel model. However, the treatment of ionic effects of the electrolyte solution in the ion-channels with the image charge approximation remains unsolved. As the inverse Debye-Hückel screening length in the solvents does not vanish fast enough in many applications, the classical expression of the reaction potential as an infinite sum [33] does not apply directly. In this paper, we will extend our previous results on image approximation to the ion-channel model in the electrolyte solution/membrane environment.

To proceed, we first start with the exact series solution of the reaction potential of a point charge located within a layered dielectric/electrolyte medium because a cell membrane is usually described by a layer embedded in electrolyte solvents. By using this solution, several approximation methods based on least squares are proposed to find the discrete image charges. Then, we derive the image approximation of the reaction field in the presence of infinite cylinder using the method in [26]. Next, combining these two results, we obtain the image approximation of the reaction field for our ion-channel model.

The organization of this paper is as follows. In Section 2, the exact solution of a layered system with ionic effects in the solvent layers is discussed. In Section 3, the approximate methods of discrete image charges are proposed in layered media. In Section 4, the approximate methods are applied to an ion-channel model, and tested by numerical examples. Conclusions are given in Section 5.
2. Series solution for a layered medium

Let us start with a classical electric potential problem. Consider a three-layer model representing the dielectric environment of a cell membrane immersed in ionic fluids, as shown in Fig. 1. The cell membrane is treated as an infinite layer (region II), separated from the bulk solvents (region I and III) by two parallel planes. A point charge $q_s$ is located at $x_s$ inside region II. As the membrane is made of hydrocarbons, it can be described by a dielectric continuum with a low dielectric constant $\varepsilon_m$; typically, $\varepsilon_m = 2$. The electric potential $\Phi_m$ in the membrane layer, i.e., in the intermediate layer, satisfies a Poisson equation [34],

$$\Delta \Phi_m(x, x_s) = -\frac{4\pi q_s}{\varepsilon_m} \delta(x - x_s),$$

(1)

where $\delta(\cdot)$ is the Dirac delta function.

The ionic solvents in areas I and III are characterized by dielectric permittivities $\varepsilon_s$ and parameters of the inverse Debye-Hückel length, $\lambda_1$ and $\lambda_2$. The potentials in these two regions are governed by the linearized Poisson-Boltzmann equation [2] under the mean field approximation [6],

$$\Delta \Phi - \lambda^2 \Phi = 0,$$

$${\lambda} = \sqrt{\frac{8\pi N_A e^2 I}{1000 \varepsilon k_B T}},$$

(2)

where $N_A$ is Avogadro’s number, $e$ is the electron charge, $I$ is the ionic con-
centration of 1 : 1 salt in the bulk solution, \( k_B \) is the Boltzmann constant and \( T \) is the temperature. We denote the potentials of these two regions by \( \Phi_{up} \) and \( \Phi_{down} \), respectively.

The potential \( \Phi_m \) inside the membrane layer can be rewritten as a sum of a Coulombic contribution \( \Phi_{coul}(x, x_s) = q_s/\varepsilon_m |x - x_s| \) and a reaction potential \( \Phi_{rf} \), due to the polarization of the ionic solvents by the source charge \( q_s \). By expanding both sides of the Poisson equation with orthonormal functions and the vanishing of the Coulombic potential at \( \infty \), the potential \( \Phi_{coul} \) can be expanded as follows,

\[
\frac{q_s}{\varepsilon_m |x - x_s|} = \int_0^{+\infty} \int_0^{+\infty} d\alpha d\beta \cos \alpha(x - x_s) \cos \beta(y - y_s) \frac{2q_s}{\varepsilon_m \pi \gamma} e^{-\gamma |z - z_s|},
\]

where \( \gamma = \sqrt{\alpha^2 + \beta^2} \). Equation (3) is a Sommerfeld-type identity well known in electromagnetic scattering theory [40][39].

As \( \Phi_{rf} \) satisfies the Laplace equation and \( \Phi_{up} \) and \( \Phi_{down} \) satisfies the linearized Poisson-Boltzmann equation (2), these three potentials can also be expanded as,

\[
\Phi_{rf}(x, x_s) = \int_0^{+\infty} \int_0^{+\infty} d\alpha d\beta \cos \alpha(x - x_s) \cos \beta(y - y_s)[A(\alpha, \beta)e^{\gamma z} + B(\alpha, \beta)e^{-\gamma z}],
\]

\[
\Phi_{up}(x, x_s) = \int_0^{+\infty} \int_0^{+\infty} d\alpha d\beta \cos \alpha(x - x_s) \cos \beta(y - y_s)C(\alpha, \beta)e^{-\sqrt{\gamma^2 + \alpha^2} z},
\]

\[
\Phi_{down}(x, x_s) = \int_0^{+\infty} \int_0^{+\infty} d\alpha d\beta \cos \alpha(x - x_s) \cos \beta(y - y_s)D(\alpha, \beta)e^{\sqrt{\gamma^2 + \alpha^2} z}.
\]

Suppose the planar surfaces are located at \( z = 0 \) and \( z = l \) with \( l \) being the thickness of the membrane. Two interface conditions for the continuities of the potential and the normal displacements at each interface are given by,

\[
\Phi_m = \Phi_{down}, \quad \varepsilon_m \frac{\partial \Phi_m}{\partial z} = \varepsilon_s \frac{\partial \Phi_{down}}{\partial z}, \quad \text{for } z = 0,
\]

\[
\Phi_m = \Phi_{up}, \quad \varepsilon_m \frac{\partial \Phi_m}{\partial z} = \varepsilon_s \frac{\partial \Phi_{up}}{\partial z}, \quad \text{for } z = l.
\]
Substituting the boundary conditions (7) and (8) into expressions (3)-(6) yields a linear system for the coefficients $A, B, C$ and $D$,

\[
\begin{cases}
2q \varepsilon_m e^{-\gamma z_s} + A + B = D, \\
2q \varepsilon_m e^{-\gamma z_s} + \gamma A - \gamma B = \frac{\varepsilon_s}{\varepsilon_m} \sqrt{\gamma^2 + \lambda_2^2} D, \\
2q \varepsilon_m e^{-\gamma (l-z_s)} + Ae^{\gamma l} + Be^{-\gamma l} = Ce^{-\sqrt{\gamma^2 + \lambda_1^2 l}}, \\
-2q \varepsilon_m e^{-\gamma (l-z_s)} + \gamma Ae^{\gamma l} - \gamma Be^{-\gamma l} = -\frac{\varepsilon_s}{\varepsilon_m} \sqrt{\gamma^2 + \lambda_1^2 l}.
\end{cases}
\]

For convenience, let $\varepsilon = \varepsilon_m$, $\tau_i = \varepsilon \sqrt{\gamma^2 + \lambda_i^2}$, $i = 1, 2$. Solving the linear system (9) leads to the coefficients in the reaction potential $\Phi_{rf}$ (4),

\[
A(\alpha, \beta) = \frac{2q e^{-\gamma (l-z) \tau_1} (\gamma + \tau_1) (\gamma + \tau_2) e^{\gamma l} - (\gamma - \tau_1) (\gamma - \tau_2) e^{-\gamma l}}{\varepsilon_m \pi \gamma (\gamma + \tau_1) (\gamma + \tau_2) e^{\gamma l} - (\gamma - \tau_1) (\gamma - \tau_2) e^{-\gamma l}}.
\]

\[
B(\alpha, \beta) = \frac{2q e^{-\gamma (l-z) \tau_1} (\gamma + \tau_1) (\gamma - \tau_2) e^{\gamma l} + e^{-\gamma (l+z) \tau_1} (\gamma - \tau_1) e^{-\gamma l}}{\varepsilon_m \pi \gamma (\gamma + \tau_1) (\gamma + \tau_2) e^{\gamma l} - (\gamma - \tau_1) (\gamma - \tau_2) e^{-\gamma l}}.
\]

3. Method of image charges in layered inhomogeneities

In this section, we will study the use of the image charge representation and approximation to the reaction field in layered inhomogeneous dielectrics/solutions.

3.1 A layered and non-ionic solution - RIC method

First, let us consider the case of pure water where no free charge is presented in the solvents (pure water), then, the inverse Debye-Hückel length $\lambda_1 = \lambda_2 = 0$. For this case, a rectangular image charge (RIC) method was used for the reaction field [33], where the reaction potential for a point charge in a rectangular infinite system was suggested as,

\[
\Phi_{rf}(x, x_s) = \sum_{k=-\infty, k\neq0}^{k=+\infty} \frac{Q_k}{\varepsilon_m |x - x_k|}.
\]
expression (4) can be rewritten into four parts as

\[ \Phi_{rf}(\mathbf{x}, \mathbf{x}_s) = \int_0^{\infty} \int_0^{\infty} d\alpha d\beta \cos \alpha(x - x_s) \cos \beta(y - y_s) [I + II + III + IV] \]

\[ I = \frac{2q}{\varepsilon_m \pi \gamma} \frac{e^{-\gamma(2l+z_s-z)} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^2}{1 - e^{-2\gamma l} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^2}, \quad II = \frac{2q}{\varepsilon_m \pi \gamma} \frac{e^{-\gamma(2l+z_s-z)} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^2}{1 - e^{-2\gamma l} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^2}, \]

\[ III = \frac{2q}{\varepsilon_m \pi \gamma} \frac{e^{\gamma(-z_s-z)} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^2}{1 - e^{-2\gamma l} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^2}, \quad IV = \frac{2q}{\varepsilon_m \pi \gamma} \frac{e^{-\gamma(2l+z_s-z)} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^2}{1 - e^{-2\gamma l} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^2}. \]

As \( e^{-2\gamma l} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^2 < 1 \), the denominator in (13) can be expanded as a geometric progression,

\[ \frac{1}{1 - e^{-2\gamma l} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^2} = \sum_{k=0}^{k=\infty} e^{-2\gamma l} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^{2k} = \sum_{k=0}^{k=-\infty} e^{2\gamma l} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^{-2k}, \]

then, (13) becomes:

\[ \Phi_{rf}(\mathbf{x}, \mathbf{x}_s) = \sum_{k=0}^{k=\infty} \int_0^{\infty} \int_0^{\infty} d\alpha d\beta \cos \alpha(x - x_s) \cos \beta(y - y_s) \frac{2q}{\varepsilon_m \pi \gamma} \left( e^{-\gamma(2k+2l+z_s-z)} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^{2k+1} + e^{-\gamma(2k+2l+z_s-z)} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^{2k+1} \right) \]

\[ + \sum_{k=0}^{k=-\infty} \int_0^{\infty} \int_0^{\infty} d\alpha d\beta \cos \alpha(x - x_s) \cos \beta(y - y_s) \frac{2q}{\varepsilon_m \pi \gamma} \left( e^{-\gamma(2l+z_s-z)} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^{-2k+1} + e^{-\gamma(-2k+2l+z_s+z)} \left( \frac{1-\varepsilon}{1+\varepsilon} \right)^{-2k+1} \right) \]

\[ = \sum_{k=0}^{k=\infty} \frac{Q_{2k+1}}{\varepsilon_m |\mathbf{x} - \mathbf{x}_{2k+1}|} + \frac{Q_{2k+2}}{\varepsilon_m |\mathbf{x} - \mathbf{x}_{2k+2}|} \]

\[ + \sum_{k=0}^{k=-\infty} \frac{Q_{2k-1}}{\varepsilon_m |\mathbf{x} - \mathbf{x}_{2k-1}|} + \frac{Q_{2k-2}}{\varepsilon_m |\mathbf{x} - \mathbf{x}_{2k-2}|} \]

\[ = \sum_{k=-\infty, k\neq 0}^{k=+\infty} \frac{Q_k}{\varepsilon_m |\mathbf{x} - \mathbf{x}_k|}. \]
where the second last equation holds from the Sommerfeld identity (3). Hence, the proof for the equivalence between the expression (4) and (12).

It should also be mentioned that image formula (12) in fact approximates the solution to the ionic case (2) with an accuracy of $O(\lambda)$ and the proof is technical, but straightforward and omitted here.

3.2 Layered ionic solutions

In this case, although the integrand in expression (4) of $\Phi_{rf}$ is damped exponentially at high frequencies, numerical integration of $\Phi_{rf}$ is still time consuming. In simulations of biological systems, image charge methods [17,18] are widely used to speed up the calculation of electrostatic interactions. In particular, the method of multiple images [22] was developed to treat the electrostatic reaction field of spherical geometries with high accuracy, which is based on a numerical quadrature of line image representation [35–37]. The key of multiple image methods is to find some image points such that their electrostatic potentials give an accurate approximation to the sought-after reaction field,

$$\Phi_{irf}(x, x_s) = \frac{q_s}{\varepsilon_m} \sum_k \frac{q_k}{|x - x_k|},$$

(14)

where unknown $q_k$ and $x_k$ are the strength and the location of the $k$th image charge with a dependence on the location $x_s$ of the unit source charge. The technique used in proving the RIC method is not applicable here as the integral become too complicated. Here, we introduce two ways to obtain the image charge approximation and present corresponding numerical test results.

In the first method, the locations of the image charges are pre-fixed at the locations given in the RIC method (12) and their magnitudes are obtained through a least square procedure. Meanwhile, in the second method, both the locations and the magnitudes of the image charges are produced through a
Prony type approximation to the Fourier transform of the reaction potential and the Sommerfeld type identity (3).

3.2.1 Method based on fitting the reaction potential with image-based potentials

Setting $N$ monitoring points inside the membrane layer, denote as $\hat{x}_n, n = 1, 2, \cdots, N$, and considering the image charges in pairs, i.e., the $k$th pair of image charges locate at $x_{\pm k}$. In order to be consistent with the RIC method, we fix $x_{\pm k}$ as

$$x_k = \left(x_s, y_s, (-1)^k \left(z_s - \frac{l}{2}\right) + \left(k + \frac{1}{2}\right) l\right), \quad k = \pm 1, \pm 2, \cdots.$$

Then, the $L_2$ error between the image-based potential field and the exact reaction field reads:

$$Err(\{q_{\pm k}\}_{k=1}^K) = \sqrt{\frac{\sum_{n=1}^N [\Phi_{irf}(\hat{x}_n, x_s) - \Phi_{rf}(\hat{x}_n, x_s)]^2}{\sum_{n=1}^N \Phi_{rf}(\hat{x}_n, x_s)^2}}$$

Solving the minimization problem yields the value of $q_{\pm k}$. In fact, as the variable $q_{\pm k}$ is only present in the numerator of the error function, the minimization problem is linear and easy to solve.

A simple Mathematica code is developed to calculate the strength of image charges for each set of dielectric parameters and Debye length, the “FindMinimum” subroutine is used to solve the minimization problem. To show the performance of the code, we set $\varepsilon_m = 1$, $\varepsilon_s = 80$, $\lambda_1 = 2.5$ and $\lambda_2 = 0.5$, here the $\varepsilon_s = 80$ represents the water dielectric, and a relative small $\varepsilon_m$ represents a dielectric constant of membrane lipids. As the origin of $x$-$y$ plane should not influence the calculation, we set the source charges at $(0, 0, z_s)$ without loss of the generality. In all calculations, we take $N = 512$ monitoring points uniformly distributed in a rectangle centered at $(0, 0, 0.5l)$, here $l$, the thickness
of membrane, is set to be \( l = 1 \) as a dimensionless parameter.

We set \( K = 2 \), i.e., four image charges are used to approximate the reaction field. Numerical tests that this choice gives satisfactory accuracy. The locations of these four image charges are

\[
x_{-2} = (0, 0, -2l + z_s), x_{-1} = (0, 0, -z_s), x_1 = (0, 0, 2l - z_s), x_2 = (0, 0, 2l + z_s).
\]

To find the systematic dependence of the image charges on the location of the source charge \( z_s \), we fit the numerical results of \( q_{\pm 1}, q_{\pm 2} \) at selected choices of \( z_s \) by an analytical function of \( \hat{z}_s = z_s/l \). Sixth order polynomials plus a term \( 1/\hat{z}_s \) are used for this purpose. The resulting image charges for a range of the fitted source location \( z_s \) gives approximation to the reaction field at the corresponding source charge within an error less than 1%. The exact dependence on \( z_s \) is summarized in the following relation.

By denoting,

\[
\vec{q} = (q_{-2}, q_{-1}, q_1, q_2)^\top, \quad \vec{Z}_s = (\hat{z}_s^6, \hat{z}_s^5, \hat{z}_s^4, \hat{z}_s^3, \hat{z}_s^2, \hat{z}_s, 1, 1/\hat{z}_s)^\top,
\]

we have

\[
\vec{q} = C_1 \vec{Z}_s, \tag{16}
\]

where

\[
C_1 = \begin{pmatrix}
58.3268 & -167.32 & 187.036 & -102.557 & 28.073 & -2.7127 & 0.2281 & -0.0035 \\
-0.1335 & 0.4557 & -0.6430 & 0.3289 & 0.3440 & -0.6359 & -0.7012 & 0.0014 \\
0.2214 & -0.6194 & 0.7137 & -0.6954 & -0.0167 & -0.3011 & 0.6732 & -0.0014
\end{pmatrix}.
\]

Figure 2 shows the difference in computing the reaction field of using the image charges at available \( z_s \) and the image charges given by the fitted function (16).
The small difference indicates that we can use image charges given by (16) for computing the reaction field for any \( z_s \) in the fitted range.

![Fig. 2. Relative errors (15) of the reaction field with four images, the solid line: images given by the fitting functions (16), and the diamonds: images obtained by minimizing (15).](image)

### 3.2.2 Method based on a Prony fitting of Fourier transform of the reaction potential

The second method to construct the image charges is based on a Prony approximation \([38,41]\), where a sum of exponentials is used to approximate the Fourier transform of the exact reaction field potential. Rewrite the exact reaction field (4) in the following form,

\[
\Phi_{rf}(\mathbf{x}, \mathbf{x}_s) = \int_{0}^{+\infty} \int_{0}^{+\infty} d\alpha d\beta \cos \alpha (x - x_s) \cos \beta (y - y_s) \frac{2q_s}{\varepsilon_m \pi \gamma} [\hat{A} e^{\gamma z} + \hat{B} e^{-\gamma z}],
\]

(17)

where

\[
\hat{A}(\gamma) = \frac{e^{-\gamma (l - z_s)}(\gamma - \tau_1)(\gamma + \tau_2) + e^{-\gamma (l + z_s)}(\gamma - \tau_1)(\gamma - \tau_2)}{(\gamma + \tau_1)(\gamma + \tau_2)e^{\gamma l} - (\gamma - \tau_1)(\gamma - \tau_2)e^{-\gamma l}},
\]

\[
\hat{B}(\gamma) = \frac{e^{\gamma (l - z_s)}(\gamma + \tau_1)(\gamma - \tau_2) + e^{\gamma (l + z_s)}(\gamma - \tau_1)(\gamma - \tau_2)}{(\gamma + \tau_1)(\gamma + \tau_2)e^{\gamma l} - (\gamma - \tau_1)(\gamma - \tau_2)e^{-\gamma l}}.
\]

(18)

Comparing this expression with the Sommerfeld identity (3), and using the symmetry of the rectangular system, a natural approach is to approximate
the function $\hat{A}(\gamma)$ and $\hat{B}(\gamma)$ by a sum of exponential functions as,

$$
\hat{A}^{\text{app}}(\gamma) = \sum_{k=1}^{K} \left( a_{2k-1} e^{-(z_{2k-1} - c_k)\gamma} + a_{2k} e^{-(z_{2k} + c_k)\gamma} \right),
$$

$$
\hat{B}^{\text{app}}(\gamma) = \sum_{k=-1}^{-K} \left( a_{2k+1} e^{(z_{2k+1} + c_k)\gamma} + a_{2k} e^{(z_{2k} - c_k)\gamma} \right),
$$

where $z_k = (-1)^k(z_s - \frac{l}{2}) + (k + \frac{1}{2})l$ are the location of image charges in the case $\lambda_1 = \lambda_2 = 0$, $a_{\pm k}, c_{\pm k}$ are unknown variations of the $k$th pair image charges.

Imposing the following conditions:

$$
z_{2k-1} - c_k > l, \quad z_{2k} + c_k > l, \quad \text{for} \quad k > 0,
$$

$$
z_{2k+1} + c_k < 0, \quad z_{2k} - c_k < 0, \quad \text{for} \quad k < 0,
$$

then applying the Sommerfeld type identity (3) yields:

$$
\Phi_{\text{irf}}(x, x_s) = \int_{0}^{+\infty} \int_{0}^{+\infty} d\alpha d\beta \cos \alpha (x - x_s) \cos \beta (y - y_s) \frac{2q_s}{\varepsilon_m \pi \gamma} \left[ \sum_{k=1}^{K} \left( a_{2k-1} e^{-(z_{2k-1} - c_k)\gamma} + a_{2k} e^{-(z_{2k} + c_k)\gamma} \right) 
+ \sum_{k=-1}^{-K} \left( a_{2k+1} e^{-(z_{2k+1} + c_k)\gamma} + a_{2k} e^{-(z_{2k} - c_k)\gamma} \right) \right] (19)
$$

$$
= \sum_{k=1}^{K} \frac{q_s}{\varepsilon_m} \frac{a_{2k-1}}{x - x_{2k-1}} + \frac{a_{2k}}{x - x_{2k}}, \quad \sum_{k=-1}^{-K} \frac{q_s}{\varepsilon_m} \frac{a_{2k+1}}{x - x_{2k+1}} + \frac{a_{2k}}{x - x_{2k}},
$$

with

$$
x_{2k-1} = (x_s, y_s, z_{2k-1} - c_k), \quad x_{2k} = (x_s, y_s, z_{2k} + c_k), \quad k > 0, \quad (20)
$$

$$
x_{2k+1} = (x_s, y_s, z_{2k+1} + c_k), \quad x_{2k} = (x_s, y_s, z_{2k} - c_k), \quad k < 0. \quad (21)
$$

Once $a_k$ and $c_k$ are found, the image charges are given by the Sommerfeld type identity (3). Fig. 3 shows the geometric meaning of $a_k$ and $c_k$. As functions $\hat{A}(\gamma)$ and $\hat{B}(\gamma)$ are smoothly damped exponentials, such an approximation is reasonable and effective. The parameter $a_k$ and $c_k$ can be calculated by solving a simple minimization problem of the $L_2$ errors, sampling $\gamma$ at $\gamma_j, j = 1, 2, \cdots, J$. The $L_2$ error of the approximate function and the exact function
We use the same parameters as the previous method: $\varepsilon_m = 1$, $\varepsilon_s = 80$, $\lambda_1 = 2.5$, $\lambda_2 = 0.5$ and $l = 1$. The source charge is supposed to locate at $(0, 0, z_s)$. Choosing $K = 1$, i.e., two exponentials to approximate each of $\hat{A}$ and $\hat{B}$. Here let $\gamma_j$ be the scaled Chebyshev interpolation points in the interval $[0, 10]$. For the choice of $J$, the number of sampling points, the Table 1 shows the decay of $L_2$ errors in terms of increasing $J$.

<table>
<thead>
<tr>
<th>$J$</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>max $z_s \in (0,l) \left{ \sum_{t=1}^{100} \frac{(\hat{A}(\frac{t}{10}) - \hat{A}_{app}(\frac{t}{10}))^2}{100} \right}$</td>
<td>0.00538</td>
<td>0.00196</td>
<td>0.00080</td>
<td>0.00068</td>
</tr>
<tr>
<td>max $z_s \in (0,l) \left{ \sum_{t=1}^{100} \frac{(\hat{B}(\frac{t}{10}) - \hat{B}_{app}(\frac{t}{10}))^2}{100} \right}$</td>
<td>0.00928</td>
<td>0.00571</td>
<td>0.00658</td>
<td>0.00630</td>
</tr>
</tbody>
</table>

Table 1. Convergence of $J$-sampling Fourier transform of reaction potential

Fig. 3. The physical meaning of $a_k$ and $c_k$, taking $k = \pm 1$ for example.
The numerical tests show $J = 10$ is a good enough choice with an overall error less than 0.1%. Again as before, by least squares fitting the data at selected $z_s$, we can obtain an analytical dependence of the coefficients on $z_s$ as follows.

Setting $\hat{z}_s = z_s/l$ and

$$\mathbf{a} = (a_1, a_2, a_{-1}, a_{-2}, c_1, c_{-1})^T, \mathbf{Z}_s = (\hat{z}_s^6, \hat{z}_s^5, \hat{z}_s^4, \hat{z}_s^3, \hat{z}_s^2, \hat{z}_s, 1)^T$$

we have

$$\mathbf{a} = C_2 \mathbf{Z}_s,$$  \hspace{1cm} (24)

where

$$C_2 = \begin{pmatrix}
-0.7897 & 3.1309 & -4.9024 & 3.5424 & -0.4660 & -1.4715 & -0.0384 \\
0.7888 & -3.1316 & 4.9043 & -3.5493 & 0.46723 & 0.5071 & 0.0130 \\
-3.5602 & 9.7702 & -9.5473 & 4.6495 & -0.5400 & 0.1877 & -0.9766 \\
3.6741 & -10.101 & 9.8343 & -4.6115 & 0.3358 & 0.8773 & 0.0030 \\
-5.7251 & 20.3875 & -28.9648 & 20.7972 & -7.5971 & 0.7714 & 0.3235 \\
-4.6749 & 12.8514 & -13.3379 & 6.6873 & -1.3877 & 0.1440 & -0.0029 \\
\end{pmatrix}.$$

Analogously, the $L_2$ error function between the image-based potential and the exact reaction field reads,

$$\text{Err}(\{a_{\pm(2k-1)}, a_{\pm 2k}, c_{\pm k}\}_{k=1}^{K}) = \left(\frac{\sum_{n=1}^{N} [\Phi_{irf}(\hat{x}_n, x_s) - \Phi_{rf}(\hat{x}_n, x_s)]^2}{\sum_{n=1}^{N} \Phi_{rf}(\hat{x}_n, x_s)^2}\right)^{\frac{1}{2}}. \hspace{1cm} (25)$$

Fig. 4 shows the difference in computing the reaction field of using the image charges at available $z_s$ and the image charges given by the fitted function (24) (20-21). The small difference indicates that we can use image charges given by (24) (20-21) for computing the reaction field for any $z_s$ in the fitted range.
Fig. 4. Relative errors of the reaction field with four images, the solid line: images given by the fitting functions (24) and (20-21), and the diamonds: images obtained by minimizing (22-23) and (20-21).

The numerical test shows that both two approximate methods provide satisfactory accuracy, while the second one is much simpler as the user only needs to deal with the integrand. The fitting functions in both methods only depend on the dielectric permittivities $\varepsilon_m, \varepsilon_s$ and Debye length $\lambda_1, \lambda_2$. The Mathematica program is available (upon request to the author) for generating such functions.

4. Method of image charges in an ion-channel model

In this section, we will construct image charge approximation to the reaction field in an ion-channel model as Fig. 5, which includes three dielectric areas: a finite cylinder, the membrane surrounding the cylinder, and the bulk solvents (upper and lower semi-infinite layers), these three areas are characterized by dielectric constants $\varepsilon_0, \varepsilon_m$ and $\varepsilon_s$, respectively. Such a model involves inhomogeneity of layered and cylindrical structures. We will handle each type individually, and then combine the results to address the ion-channel inhomogeneity.
First, for the infinite cylinder system, see Fig. 6, consider a point charge $q_s$ located at position $r_s$ inside the cylinder, denote the radius of the cylinder as $a$, the cylinder partitions the whole space into two regions, characterized by $\varepsilon_0$ and $\varepsilon_m$.

According to [26], the reaction potential of point charge $(q_s, r_s)$ can be approximated as

$$\Phi_{\text{cylinder}}(r, r_s) = \frac{q_s}{\varepsilon_0} \sum_{c=1}^C \frac{f_c}{| r - x_c |}. \quad (26)$$

Suppose $r_s = (\rho_s, \varphi_s, z_s)$ under the cylindrical coordinate system. Here $x_c = (\rho_c, \varphi_s + \varphi_c, z_s)$, $f_c, \rho_c, \varphi_c$ can be generated by a function depending on $\varepsilon_0$ and $\varepsilon_m$. Especially, if $\varepsilon_0 = 1$, $\varepsilon_m = 2$, and $C = 3$, the three image charges are $(f_c, \rho_c, \varphi_c) = \{(f_1, \rho_1, 0) ; (f_2, \rho_2, \pm \varphi_2)\}$. Let $p = \rho_s /a$, we have the following dependence of the image charges on the location of the source charge $\rho_s$ [26].
Setting
\[ \overrightarrow{f} = (f_1, \rho_1/a, f_2, \rho_2/a, \varphi_2)^T, \overrightarrow{p} = (p^5, p^4, p^3, p^2, p, 1)^T \]
we have
\[ \overrightarrow{f} = C_3 \overrightarrow{p}, \quad (27) \]
where
\[
C_3 = \begin{pmatrix}
0.6017 & -0.3404 & -0.3575 & 0.1087 & -0.1786 & -0.2056 \\
0.1325 & -0.9731 & 0.9896 & -0.4172 & -0.2402 & 1.5140 \\
-0.5329 & 0.6471 & -0.1531 & 0.0826 & 0.0790 & -0.2065 \\
5.0993 & -8.5071 & 5.0090 & -1.5284 & 0.2496 & 1.5133 \\
\end{pmatrix}.
\]

Now we will combine this result with the results of layered media in previous section to address the inhomogeneity of the the ion-channel model in Fig. 5.

Let us assume that the source charge \( q_s \) is at \( r_s = x_0 = (\rho_0, \varphi_0 + \varphi, z_s) \) inside an infinite cylinder with a radius of the ion channel size \( a \). The dielectric constant inside the cylinder is that of the cavity (close to 1-2) and the dielectric constant outside the cylinder is taken as that of the membrane. The cylindrical interface will require the following image charges \( f_c q_s, c = 1, \ldots, C \) for the approximation of the reaction field potential as in (26). Now, we introduce the planar membrane/solvent interfaces at \( z = 0, l \), which will generate \( 2K \) image charges \( q_s q_k \) and \( f_c q_s q_k, k = \pm 1, \ldots, \pm K \) for the approximation of the reaction field as in (14) for each of the charges \( q_s \) and \( f_c q_s \). Altogether, the reaction field for the ion-channel model can now be approximated by the potential of \( (2K + 1)(C + 1) - 1 \) image charges as
\[
\Phi_{rf}(r, r_s) \approx \frac{q_s}{\varepsilon_0} \sum_{c=0}^C \sum_{k=-K}^K \frac{(1 - \delta_{c0} \delta_{k0}) f_c q_k}{|r - x_{c,k}|}, \quad (28)
\]
where $\mathbf{x}_{c,k}$ is the image charge point given in (14) indexed by $k$ in rectangular infinite system for the source charge located at $\mathbf{x}_c$.

**Remark 1** Notice that (28) is obtained under the assumption the medium between the planes is homogenous, which implies that we have to ignore the difference in the dielectric constants of the membrane and the interior of the cylinder (chosen close to the vacuum). This is justified as both of them are small compared to the dielectric constant of the solvents ($\sim 80$).

The accuracy of the image solution (28) is tested by calculating the self energy $V(\mathbf{r}) = q_s \Phi_{rf}(\mathbf{r})/2$ of a unit point charge located within the finite cylinder. The radius and the height of the cylinder is $4 \text{ Å}$ and $12 \text{ Å}$. At first, we set the source charge at $(x, 0, z)$, where $x$ takes two values, 0 and $2 \text{ Å}$, and $z$ varies from 3 to $9 \text{ Å}$. For a reference solution, the Poisson-Boltzmann equation is solved by a 3D finite difference method in [42] for the ion-channel model with uniform grids of size $h = 0.5 \text{ Å}$.

Let $\varepsilon_0 = 1$, $\varepsilon_m = 2$, $\varepsilon_s = 80$, $\lambda_1 = 2.5$ and $\lambda_2 = 0.5$ in the ion-channel model, so that the expression (16), (24) and (27) can be applied directly. Figs. 7 and 8 give the comparative result on self energies between the image-based (28) and finite difference method. As 4 images are used to treat the planner interface inhomogeneity and 3 images are used for the cylindrical interface inhomogeneity, this results in a 19 images being used in the image approximation to the reaction field (28) for the ion-channel model. In Figs. 7 and 8, method 1 stands for images obtained in Section 3.2.1, and method 2 stands for images obtained in Section 3.2.2. In Figure 7, the relative errors are less than 3% for method 1 and 4% for method 2, and in Figure 8, the maximum error is about 4%. Fig. 10 plots the result for the charge located at $(x, 0, 1)$ (close to the interface between the cylinder and the bottom plane), it shows that the image charge method is accurate even for charges close to the boundary.
5. Concluding remarks

Image approximations to the electrical potential in the Poisson-Boltzmann theory for electrolyte solutions and dielectrics in inhomogeneous media such as layered or cylindrical structure are obtained and found to be an accurate and
efficient numerical method. Furthermore, the image approximation for the ion-channel configuration will allow the application of hybrid solvation model with a reaction field based molecular dynamics simulation [13] for the selectivity of various ion-channels. The image approximation to the reaction field removed the inhomogeneity of the system such that all electrostatic interactions in the ion-channel and ionic solvent/membrane environment are expressed in terms of Coulombic pairwise interactions between source charges and their image charges. As a result, fast algorithms such as the FMM can be used to produce a linear scaling algorithm in treating the electrostatics interactions for molecular simulations of ion-channels, on which research is underway.

Appendix: Series expansion for a general multi-layered system

For a general multi-layered model, which is schematically shown in Figure 11, the system is divided into several rectangular infinite regions, indexed by $\Omega_i$, $i = -m - 1, -m, \cdots, n + 1$. The dielectric constant and the Debye length are constant in each area $\Omega_i$, denoted as $\varepsilon_i$ and $\lambda_i$, a source charge $q_s$ at $x_s$ is inside $\Omega_0$. Denoting the electric potential in $\Omega_i$ as $\Phi_i$, in layer $\Omega_0$, $\Phi_0$ satisfies
the Poisson equation \[34\],
\[ \triangle \Phi_0(x, x_s) = -\frac{4\pi q_s}{\varepsilon_0} \delta(x - x_s). \tag{29} \]

Meanwhile, for area \( \Omega_i, i \neq 0 \), \( \Phi_i \) satisfies the linearized Poisson-Boltzmann equation \[2\],
\[ \triangle \Phi_i - \lambda_i^2 \Phi_i = 0. \tag{30} \]

Analogously, \( \Phi_0 \) can be rewritten as a sum of the Coulombic contribution \( \Phi_{\text{coul}} = q_s/\varepsilon_0|x - x_s| \) and a reaction potential \( \Phi_{\text{rf}} \). The following expansions hold,
\[ \Phi_{\text{coul}}(x, x_s) = \int_0^{+\infty} \int_0^{+\infty} d\alpha d\beta \cos\alpha(x - x_s) \cos\beta(y - y_s) \frac{2q_s}{\varepsilon_0 \pi \gamma} e^{-\gamma |z - z_s|}, \tag{31} \]
\[ \Phi_{\text{rf}}(x, x_s) = \int_0^{+\infty} \int_0^{+\infty} d\alpha d\beta \cos\alpha(x - x_s) \cos\beta(y - y_s) \left[A_0 e^{\gamma z} + B_0 e^{-\gamma z}\right], \tag{32} \]
\[ \Phi_i(x, x_s) = \int_0^{+\infty} \int_0^{+\infty} d\alpha d\beta \cos\alpha(x - x_s) \cos\beta(y - y_s) \left[A_i e^{\sqrt{\gamma^2 + \lambda_i^2} z} + B_i e^{-\sqrt{\gamma^2 + \lambda_i^2} z}\right], \tag{33} \]
\[ i \neq 0, \quad B_{-m-1} = 0, \quad A_{n+1} = 0. \]

Suppose that the surface \( \Gamma_i \) locates at \( z = il, i = -m - 1, -m, \cdots, n + 1, l \) is the thickness of the layer \( \Omega_0 \). At each surface \( \Gamma_i \), two interface conditions hold,
\[ \Phi_{i-1} = \Phi_i, \quad \varepsilon_{i-1} \frac{\partial \Phi_{i-1}}{\partial z} = \varepsilon_i \frac{\partial \Phi_i}{\partial z}, \quad \text{on } \Gamma_i. \tag{34} \]

Substituting the boundary conditions (34) into the expansions yields a linear
system for the coefficients $A_i$ and $B_i$,

$$
\begin{align*}
A_{-1} + B_{-1} &= \frac{2q}{\varepsilon_0 \gamma} e^{-\gamma z} + A_0 + B_0, \\
\varepsilon_{-1} \sqrt{\gamma^2 + \lambda_{-1}^2} (A_{-1} - B_{-1}) &= \frac{2q}{\varepsilon_0 \gamma} e^{-\gamma z} + \varepsilon_0 \gamma A_0 - \varepsilon_0 \gamma B_0, \\
A_1 e^{\sqrt{\gamma^2 + \lambda_1^2} l} + B_1 e^{-\sqrt{\gamma^2 + \lambda_1^2} l} &= \frac{2q}{\varepsilon_0 \gamma} e^{-\gamma (l-z)} + A_0 e^{\gamma l} + B_0 e^{-\gamma l}, \\
\varepsilon_{1} \sqrt{\gamma^2 + \lambda_1^2} \left(A_1 e^{\sqrt{\gamma^2 + \lambda_1^2} l} - B_1 e^{-\sqrt{\gamma^2 + \lambda_1^2} l}\right) &= \frac{2q}{\varepsilon_0 \gamma} e^{-\gamma (l-z)} + \varepsilon_0 \gamma A_0 e^{\gamma l} - \varepsilon_0 \gamma B_0 e^{-\gamma l}, \\
A_{i-1} e^{i \sqrt{\gamma^2 + \lambda_{i-1}^2} l} + B_{i-1} e^{-i \sqrt{\gamma^2 + \lambda_{i-1}^2} l} &= A_i e^{i \sqrt{\gamma^2 + \lambda_i^2} l} + B_i e^{-i \sqrt{\gamma^2 + \lambda_i^2} l}, \\
\varepsilon_{i-1} \sqrt{\gamma^2 + \lambda_{i-1}^2} \left(A_{i-1} e^{i \sqrt{\gamma^2 + \lambda_{i-1}^2} l} - B_{i-1} e^{-i \sqrt{\gamma^2 + \lambda_{i-1}^2} l}\right) &= \varepsilon_i \sqrt{\gamma^2 + \lambda_i^2} \left(A_i e^{i \sqrt{\gamma^2 + \lambda_i^2} l} - B_i e^{-i \sqrt{\gamma^2 + \lambda_i^2} l}\right), \\
A_{n+1} &= 0, \quad B_{-m-1} = 0, \quad i = -m, -m + 1, \cdots, -1, \text{ and } 2, 3, \cdots, n.
\end{align*}
$$

Solving this linear system would give the desired expansion for each $\Phi_i$.

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