A novel formulation of nonlocal electrostatics

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The accurate modeling of the dielectric properties of water is crucial for many applications in physics, computational chemistry and molecular biology. This becomes possible in the framework of nonlocal electrostatics, for which we propose a novel formulation allowing for numerical solutions for the nontrivial molecular geometries arising in the applications mentioned before. Our approach is based on the introduction of a secondary field, ψ, which acts as the potential for the rotation free part of the dielectric displacement field D. For many relevant models, the dielectric function of the medium can be expressed as the Green’s function of a local differential operator. In this case, the resulting coupled Poisson (-Boltzmann) equations for ψ and the electrostatic potential φ reduce to a system of coupled PDEs. The approach is illustrated by its application to simple geometries.

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The theory of continuum electrostatics plays a major role in the determination of solvation free energies of atoms, ions, and biomolecules [1]. Recent progress in its applicability to biological systems has been impressive: the electrostatic potentials of large biomolecules such as, e.g., microtubuli and ribosomes, can be determined [2]. Unfortunately, the standard continuum approach ultimately becomes inaccurate when used to determine electrostatic properties on atomic scales [3], as it is featureless, i.e., the correlation between solvent arrangements and the geometrical structure of biomolecular assemblies is not taken into account. On the other hand, continuum electrostatics is still much more efficient from a computational point of view than microscopic simulations based on, e.g., molecular dynamics (MD). Therefore, interest has risen recently in extensions of the theory of continuum electrostatics that allow to account for spatial variations of the dielectric behaviour of the solvent, in particular near boundaries [1,4]. Part of the motivation for such approaches stems from the field of protein docking, where a realistic and efficient modelling of solvent properties is essential [3].

Within the continuum theory of electrodynamics, spatial dispersion effects can be taken into account in an approach called ‘nonlocal electrostatics’ [2,5,6,7,8]. It rests on the assumption of a linear relationship between the dielectric displacement field and the electric field mediated by a permittivity kernel depending on two spatial arguments,

\[ D(r) = \varepsilon_0 \int dr' \varepsilon(r,r')E(r') \]  \hspace{1cm} (1)

where \( \varepsilon(r,r') \) is the dielectric permittivity tensor. Equivalently to eq.1, one can express the nonlocal relationship in terms of the polarization fields \( \lambda \).

While the theory of nonlocal electrostatics remains firmly embedded within the well-understood framework of Maxwell’s theory, it introduces a new characteristic length scale absent in local electrostatics: the correlation length λ of the polarization correlations between the solvent molecules. This length sets the relevant scale for the deviation of the dielectric properties of the solvent from its bulk value. Thus, nonlocal electrostatics is a serious candidate for a more realistic description of solvent properties, provided it is also computationally tractable. It is here where the difficulties arise, however. The theory of nonlocal electrostatics, discussed in detail below, is technically considerably more demanding than local electrostatics, since it is usually formulated as a system of coupled integro-differential equations. Consequently, it has so far only been applied to idealized situations, and even then typically after introducing additional approximations in order to obtain analytical results [10,11]. For complex geometries, the solution of the equations by numerical methods becomes a formidable task.

Thus, a reformulation of the equations of nonlocal electrostatics is needed in order to make the theory applicable to real-world problems. Here we present a scheme which allows to rewrite the theory in terms of a system of partial differential equations for the local fields which consequently makes it amenable to standard methods of numerical analysis. This derivation relies on two assumptions which are typically valid for e.g. the discussion of solvation problems for biomolecules: (i) the linearity of the relationship between dielectric response and the electric field, and (ii) the representation of the dielectric function in terms of Green functions of known differential operators. We first derive the set of equations, and then illustrate how to solve them on (simple) examples.

In the following we consider the situation given in Fig-
A domain \( \Omega \) (which represents a molecule) is embedded in the solvent \( \Sigma \) which takes up the whole space except \( \Omega \). The surface of the embedded domain is denoted by \( \Gamma \). Within \( \Omega \), the dielectric properties are assumed to be local, i.e., \( \varepsilon \equiv \varepsilon_{\Omega} \), while in the solvent space \( \Sigma \), eq. (1) holds. On large scales, i.e., when \(|r - r'| \gg \lambda \), the dielectric response in the solvent is again local with the bulk dielectric constant \( \varepsilon_{\Sigma} \) (with, e.g., \( \varepsilon_{\Sigma} \approx 80 \) for water). In this situation the standard equations of nonlocal electrostatics read as

\[
\Delta \phi_{\Omega} = -\frac{1}{\varepsilon_{\Omega}(r)} \rho, \quad r \in \Omega \tag{2}
\]

where \( \rho \) is the density of fixed charges which are assumed to lie confined within \( \Omega \), \( \Gamma \), which is usually the case for biomolecules in solution. This is no restriction on the validity of our approach: the existence of surface charges on \( \Gamma \) only slightly modifies the boundary conditions. Eqs. (2,3) are the Poisson equations for the geometry of Fig. 1. The primed symbol \( \nabla' \) denotes the differentiation with respect to \( r' \). Without surface charges on \( \Gamma \), the boundary conditions to eqs. (2,3) for the normal (n) and tangential (t) components of the electric and dielectric displacement field on the boundary \( \Gamma \) are given by

\[
\mathbf{D}_{\Omega,n} = \mathbf{D}_{\Sigma,n}, \quad \mathbf{E}_{\Omega,t} = \mathbf{E}_{\Sigma,t} \tag{4}
\]

where, by virtue of eq.(3), the boundary condition for \( \mathbf{D} \) is also nonlocal.

In order to step over from the integro-differential to a purely differential formulation we introduce, in addition to the potential field \( \phi \), another potential field \( \psi \) within both compartments \( \Omega \) and \( \Sigma \). Attempts similar in spirit, but differing in the implementation, have been discussed before in the literature [12], again resulting in systems of integro-differential equations. In \( \Omega \) we define the relations between the potentials \( \phi \) and \( \psi \) and the physical fields as

\[
\mathbf{E}_{\Omega} \equiv -\nabla \phi_{\Omega}, \quad \mathbf{D}_{\Omega} \equiv -\nabla \psi \tag{5}
\]

while in \( \Sigma \) we have

\[
\mathbf{E}_{\Sigma} \equiv -\nabla \phi_{\Sigma,1} \tag{6}
\]

while the dielectric displacement field in \( \Sigma \) can be represented in terms of a scalar and a vector field [14],

\[
\mathbf{D}_{\Sigma} \equiv -\varepsilon_0 \int_{\Sigma} \nabla' \varepsilon(r',r') \nabla' \phi_{\Sigma} \equiv -\nabla \psi_{\Sigma} + \nabla \times \xi_{\Sigma} \tag{7}
\]

The scalar field \( \psi \) thus serves as the potential of the rotation free part \( \mathbf{D} = -\nabla \psi_{\Sigma} \) of the dielectric displacement field \( \mathbf{D} \). In our setting \( \phi_{\Sigma} \) is determined by \( \psi_{\Sigma} \) alone, and neither \( \psi_{\Sigma} \) nor \( \phi_{\Sigma} \) are affected by \( \xi_{\Sigma} \). Note that \( \xi_{\Sigma} \) can of course be computed from e.g. eq. (4) as soon as \( \phi_{\Sigma} \) is known. Since we here are interested only in the electrostatic potential \( \phi \) and quantities derived from it, we will ignore \( \xi_{\Sigma} \) in the following.

With these definitions, the differential equations and boundary conditions, eqs. (2,3,4) can be brought into the form

\[
\Delta \psi_{\Omega} = -\rho, \quad r \in \Omega, \quad \Delta \psi_{\Sigma} = 0, \quad r \in \Sigma \tag{8}
\]

and

\[
\nabla \psi_{\Sigma}|_n = \nabla \psi_{\Omega}|_n, \quad r \in \Gamma, \quad \nabla \phi_{\Sigma}|_t = \nabla \phi_{\Omega}|_t, \quad r \in \Gamma \tag{9}
\]

In addition, there are now two equations relating the potential fields \( \phi \) and \( \psi \),

\[
\varepsilon_0 \varepsilon_{\Omega} \phi_{\Omega} = \psi_{\Omega}, \quad r \in \Omega \tag{10}
\]

and eq.(4), to be fulfilled in \( \Sigma \).

So far, the introduction of \( \psi \) has made it possible to rewrite the boundary conditions in a completely local way. The nonlocal problem now only is with eq.(7) in which the nonlocal integral kernel still remains. The latter expression can be simplified further under additional assumptions on the explicit form of \( \varepsilon(r,r') \). We now assume that it can be written in the form

\[
\varepsilon(r,r') = \varepsilon_\ell \delta(r-r') + \tilde{\varepsilon}G(r,r') \tag{11}
\]

where \( \tilde{\varepsilon} = (\varepsilon_{\Sigma} - \varepsilon_\ell)/\lambda^2 > 0 \), and the Green function \( G \) solves

\[
\mathcal{L} \mathcal{G}(r,r') = -\delta(r-r') \tag{12}
\]

for a differential operator \( \mathcal{L} \) with constant coefficients. Note that \( \varepsilon_\ell \) refers to the value of the dielectric function on smallest scales (i.e., \( r \to r' \)) and can be related to the frequency spectrum of the dielectric function [3]. While this construction clearly restricts the theory of nonlocal electrostatics to a certain class of dielectric functions,
this restriction is not problematic as it applies to most situations of physical interest.

Under these assumptions the application of the differential operator $\mathcal{L}$ to eq. (14) yields

$$
\varepsilon_0 \left[ \varepsilon \mathcal{L} - \tilde{\varepsilon} \right] \nabla \phi_\Sigma = -\mathcal{L} \nabla \psi_\Sigma .
$$

(13)

As the fields $\phi$ and $\psi$ are determined only up to an arbitrary constant, we can drop the gradients on both sides of eq. (13) and are then left with the expression

$$
\varepsilon_0 \left[ \varepsilon \mathcal{L} - \tilde{\varepsilon} \right] \phi_\Sigma = -\mathcal{L} \psi_\Sigma .
$$

(14)

Eqs. (8 - 10, 14) constitute the novel formulation of nonlocal electrostatics based entirely on partial differential equations.

In order to apply the equations to specific physical situations, the nonlocal dielectric function and thus the Green function of the differential operator $\mathcal{L}$ need to be determined. To keep the computations simple – since here we focus only on the basic conceptual features of our approach – we further assume that the dielectric function is isotropic, i.e., $\varepsilon(r, r') = \varepsilon(r - r')$, which is exact far from any boundary. The use of more general expressions is clearly permitted in our theory and is in fact needed for the treatment of realistic situations [13, 15, 16]. Within our approach, they lead to more complex Green functions and corresponding differential operators, and will be discussed in a detailed study later.

A standard model for an isotropic nonlocal dielectric function is given by the so-called Fourier-Lorentzian model with a Yukawa-type kernel in real space. The corresponding Green function reads

$$
\mathcal{G}(r - r') = \frac{1}{4\pi |r - r'|} e^{-\frac{|r - r'|}{\lambda}}
$$

(15)

with the differential operator $\mathcal{L}$ being given by $\mathcal{L} \equiv \Delta - 1/\lambda^2$. With this choice eq. (14) reads

$$
\varepsilon_0 \left[ \varepsilon \lambda^2 \Delta - \varepsilon_\Sigma \right] \phi_\Sigma = \psi_\Sigma
$$

(16)

Note that due to $\Delta \psi_\Sigma = 0$, no differential operator appears on the rhs of eq. (16).

This result is interesting for two reasons. First, it illustrates that in the limit $\lambda \rightarrow 0$, i.e. on length scales large compared to the scale of the orientational correlations, the local limit is recovered. Second, for the differential operator chosen, the form of the equation is apparently that of a Debye-Hückel equation in which the role of the Debye-Hückel screening length is played by the combination $\lambda \varepsilon_\Sigma / \varepsilon_\Sigma^{1/2}$. And the potential $\psi$ plays the role of the density of mobile charges. We can thus interpret $\psi$ as a density of polarization charges in the bulk whose gradient gives rise to the rotation free part of the displacement field $\mathbf{D}$.

We now turn to illustrate how our formulation of nonlocal electrostatics can be put to use. First, we consider the simplest case of a charge $q$ placed at the center of a spherical shell of radius $a$. Inside the shell, we assume $\varepsilon_\Omega = 1$. This system serves as a model for ion solvation [9]. The equations for $\psi$ and $\phi$ can now be solved as follows. In the nonlocal case, the role of the Poisson equation for $\phi$ is taken over by the equation for $\psi$ according to eqs. (8, 9). The $\psi$-potential inside the shell is given by $\psi_\Sigma = 2q/r$, with the same form given outside, $\psi_\Sigma = \frac{q}{4\pi r}$. The tangential boundary condition is trivially fulfilled, while the normal boundary condition at $r = a$ leads to $q = q'$. Due to the radial symmetry of the problem, eq. (16) reads

$$
\varepsilon_0 \left[ \varepsilon \lambda^2 \left( \frac{1}{r^2} \frac{\partial}{\partial r} \left( r^2 \frac{\partial}{\partial r} \right) \right) - \varepsilon_\Sigma \right] \phi_\Sigma = \frac{q}{4\pi r}
$$

(17)

which is solved by

$$
\phi_\Sigma(r) = \frac{1}{4\pi \varepsilon_\Sigma \varepsilon_0} \frac{q}{r} (1 + A \exp(-\gamma r))
$$

(18)

where the coefficients $A$ and $\gamma$ follow from coefficient matching and the continuity of $\phi$ at the boundary, $\phi_\Sigma(a) = \phi_\Omega(a)$

$$
A = \frac{\varepsilon_\Sigma - \varepsilon_i \sinh \nu}{\varepsilon_i - \nu}, \quad \nu = \sqrt{\frac{\varepsilon_\Sigma a}{\varepsilon_i \lambda}}, \quad \gamma = \frac{\nu}{a} = \sqrt{\frac{\varepsilon_\Sigma}{\varepsilon_i \lambda}}
$$

(19)

The electrostatic potential can be used to estimate the solvation energy of monovalent and divalent ions. From $\phi_\alpha(r)$ and $\psi_\alpha(r)$, with $\alpha \in \{\Omega, \Sigma\}$, we can easily compute the free energy of solvation for this setting as the difference of the electrostatic energies in water and vacuum (where the local computation of course remains valid) from $\Delta G = \frac{1}{2} \int \{ \rho \phi - \rho \phi_{\text{vac}} \} dr$, where the integrals are split into integrals over $\Omega$ and $\Sigma$.

The result of this calculation is shown in Figure 2, where we have compared our results to a corresponding local computation (the Born-model). The correlation length $\lambda$ serves as an adjustment parameter; it is the only one in the theory. Like the ion radii, it can also be obtained from microscopic simulations. Our result compares favourably to the experimental data taken from [17]. The value for $\lambda$ was taken to be 2$\text{A}$ for the ion radii. We chose the values according to Aqvist [11]. We also tested the set of Shannon radii [19, 20] without significant differences on our results. A detailed discussion of the choice of ion radii within nonlocal electrostatics can be found in [21].
the use of cylindrical coordinates. At a point $P$ inside $\Omega$, the local dielectric medium, the electrostatic potential $\phi$ is given by
\[
\phi_{\Omega}(\rho, z) = \frac{-1}{4\pi \varepsilon_{\Omega}} \left( \frac{1}{R_1} + \frac{1}{R_2} \right)
\]
where $R_1 = \sqrt{\rho^2 + (d - z)^2}$ and $R_2 = \sqrt{\rho^2 + (d + z)^2}$ are the lengths of the vectors pointing from the charge $q$ located at $z = d$, and the image charge $q'$ at $z = -d$ to the point $P$. Inside the charge-free halfspace $\Sigma$ the potential is given by
\[
\phi_{\Sigma} = \frac{1}{4\pi \varepsilon_{\Sigma}} \frac{q''}{R_1''}
\]
with the image charge $q''$. The application of the boundary conditions for the normal and tangential components then yields the relations between the image charges $q + q' = \frac{1}{\varepsilon_{\Omega}} q''$, $q - q' = q''$ so that the potential is determined explicitly in both halfspaces. Inside $\Omega$, e.g., one has
\[
\phi_{\Omega}(\rho, z) = \frac{q}{4\pi \varepsilon_{\Omega}} \left( \frac{1}{R_1} + \frac{\varepsilon_{\Omega} - \varepsilon_{\Sigma}}{\varepsilon_{\Omega} + \varepsilon_{\Sigma}} \frac{1}{R_2} \right)
\]  
(20)

In the nonlocal case, the eqs. for $\psi$ have the same form as those for $\phi$ in the local case, so we assume the solutions to be similar. Under this assumption, the normal boundary condition remains unchanged while the tangent boundary condition leads to
\[
\partial_{\nu} \phi_{\Sigma} = \frac{1}{4\pi \varepsilon_{\Omega}} \left( \frac{q + q'}{\sqrt{q^2 + d^2}} \right)^{3/2}
\]
(21)
at $z = 0$. This equation can be readily integrated along $\theta$ and determines the potential at the dielectric boundary. For $\rho, z \to \infty$, on the other hand, $\phi_{\Sigma}$ must vanish. These two conditions then allow to compute the potential $\phi_{\Sigma}$ from eq. (10) within $\Sigma$. Since this requires a numerical computation, we leave it for a future publication where we discuss the numerical treatment of our equations. Here, we only give the lowest order effect nonlocality within $\Sigma$ has on $\Omega$. For $\rho \ll \sqrt{2d}$, the electrostatic potential inside $\Omega$ has the same form as in the local theory, but with a ‘renormalized’ bulk value of the dielectric function $\varepsilon_{\Sigma} = \varepsilon_{\Sigma, loc} - 2\varepsilon_{\Sigma}(X^2/d^2)$. Transverse variations of the permittivity in the nonlocal medium thus induce a change of the local permittivity proportional to $(\lambda/d)^2$ in the vicinity of the boundary, an effect which vanishes for $\lambda \to 0$, and for deeply buried charges, $d \to \infty$.

As a final remark on the applications of the nonlocal theory of electrostatics we mention the case in which mobile charges are present in the medium surrounding the cavity. Within the linear mean-field theory of local electrostatics, they can be described by Poisson-Boltzmann theory. This stays true within the nonlocal theory presented here. The Boltzmann distribution of the charges simply modifies the rhs of eq. (5). The nonlocal approach can then e.g. be used to quantify recent experimental results of AFM measurements on force-deflection curves at charged mica substrates in water and solutions of mono-valent ions [22]. Within a simplified treatment of the dielectric function of water, the orientational effects governed by $\lambda$ are found to be on the order of 10 nm [23]. We expect that a more realistic structural model for water, which will become computationally tractable due to our approach, will lead to a much improved description of water orientation near charged surfaces, at least in cases where the assumption of mean-field behaviour is justified.

To conclude, we have presented a novel formulation of nonlocal electrostatics, which includes the effects of spatial dispersion in the dielectric permittivity on surfaces embedded in a solvent, by reformulating it in terms of a two-potential model. While the resulting equations still need to be solved numerically even for simple geometries, this task can now be performed by standard methods developed for partial differential equations. Due to the generality of eq. (14), dielectric functions of greater complexity than the simple radially symmetric choice used here for illustrative purposes can be treated, provided they can be related to known Green functions. Work in this direction is under way.

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