Analysis of a Nonlocal Poisson-Boltzmann Equation *

L. Ridgway Scott † Dexuan Xie ‡

Abstract

A nonlinear, nonlocal dielectric continuum model, called the nonlocal modified Poisson-Boltzmann equation (NMPBE), has been proposed to reflect the spatial-frequency dependence of dielectric permittivity in the calculation of electrostatics of ionic-solvated biomolecules. However, its analysis is difficult due to its definition involving Dirac delta distributions for modeling point charges, exponential nonlinear terms for ionic concentrations, and convolution terms for dielectric corrections. In this paper, these difficulties are overcome through using a solution decomposition, a non-symmetric representation of the variational problem, and a transformation to a variational system without any convolution involved. NMPBE is then proved to be a well posed mathematical model. This analysis establishes a foundation for the numerical solution and application of NMPBE.

Keywords: nonlocal dielectric model, Poisson-Boltzmann equation, biomolecular electrostatics, solution existence and uniqueness
AMS 2000 Mathematics Subject Classifications: 35J66, 35Q92, 92-08

1 Introduction

Since the early investigations by Dogonadze and Kornyshev about four decades ago [11, 12, 22], significant progress has been made on nonlocal dielectric continuum models and their numerical solvers [2, 3, 4, 5, 7, 10, 18, 20, 25, 27, 28, 30, 32, 36, 40, 42]. As a continuation of these efforts, we recently proposed a general nonlocal Poisson dielectric continuum model [41], and then modified the classic Poisson-Boltzmann equation (PBE) as the first nonlinear and nonlocal dielectric model, called the nonlocal modified Poisson-Boltzmann equation (NMPBE), to reflect the spatial-frequency

*This work was partially supported by the National Science Foundation, USA, through grants DMS-1226259 and DMS-1226019.

†Departments of Computer Science and Mathematics, The Institute of Biophysical Design, and the Computation Institute, University of Chicago, Chicago, IL 60637 (ridg@cs.uchicago.edu)

‡Department of Mathematical Sciences. University of Wisconsin-Milwaukee, Milwaukee, Wisconsin, USA, 53201-0413 (dxie@uwm.edu)

dependence of dielectric permittivity in the calculation of electrostatics of ionic solvated biomolecules [39]. Note that PBE has been widely applied to biomolecular simulation, rational drug design, and many bioengineering problems [1, 14, 15, 26, 38]. As a nonlocal variant of PBE, NMPBE is expected to work better than PBE in the calculation of electrostatics of ionic solvated biomolecules, especially in some difficult biomolecular application problems (such as ion channel study and computer-aided drug design). But, to turn NMPBE into a valuable tool in practice, many theoretical and numerical studies have to be done. So far, we developed an effective finite element algorithm and a software package for solving NMPBE numerically [39]. The purpose of this paper is to prove that NMPBE is a well-posed mathematical model to establish a foundation for the numerical solvers and applications of NMPBE.

It is difficult to analyze NMPBE since the definition of NMPBE involves Dirac delta distributions for modeling atomic point charges of a protein molecule, exponential nonlinear terms for ionic concentrations, and nonlocal convolution terms for dielectric corrections. To overcome these difficulties, one key step of our analysis is to split the solution of NMPBE as a sum of three component functions, denoted by G, Ψ, and $\tilde{\Phi}$, with G being a known function that collects all the singular points of the NMPBE solution and both Ψ and $\tilde{\Phi}$ being twice continuously differentiable within protein region D_p and solvent region D_s, respectively. In this way, we can carry out an analysis of NMPBE through studying two component functions Ψ and $\tilde{\Phi}$ without involving any singularity difficulty.

In particular, we will employ a solution decomposition (see (3)) proposed in [39] for our analysis. In this case, Ψ is defined by a linear nonlocal interface problem (see (5)) while $\tilde{\Phi}$ is set as a solution of a nonlinear nonlocal interface problem (see (6)). We note that in the case of PBE, three different PBE solution decomposition formulas were reported in [8, 9, 38]. The one reported in [9] is very different from the other two since it splits the solution u of PBE as a sum of two functions within the protein region D_p only. The differences between the two PBE solution decompositions reported in [8, 38] mainly occur in the definitions of Ψ and $\tilde{\Phi}$. In [8], PBE was defined by an elliptic boundary value problems with discontinuous piecewise coefficients, which makes sense only in the variational form. Thus, both Ψ and $\tilde{\Phi}$ were defined only in variational forms, along with boundary value conditions different from the one from [38]. In contrast, PBE was treated as an interface problem in differential form in [38]. It was then directly split into three differential subproblems for defining G, Ψ, and $\tilde{\Phi}$ from the point view of physics and computation. That is, the three component functions G, Ψ, and $\tilde{\Phi}$ reflecte the electrostatic potentials caused by the atomic charges of a protein molecule in a solute region being the whole space $\mathbb{R}^3$, the electrostatics from the interface and boundary, and the ionic charges from the solvent region, respectively. Here a homogenous boundary value condition is enforced in the definition of $\tilde{\Phi}$ for the purpose of simplifying calculation. Since NMPBE contains PBE as a special case, its solution decomposition can immediately follow the PBE solution decomposition reported in [38].

To overcome the difficulties caused by the nonlocal convolution terms, we next treat the convolutions of Ψ and $\tilde{\Phi}$ as two unknown functions. This treatment allows us to reformulate the linear and nonlinear nonlocal interface problems (see (5) and (6)) into two systems of coupled partial differential equations (PDEs), respectively. Because the gradients of component functions Ψ and $\tilde{\Phi}$ have jump discontinuities across an interface between the solute and solvent regions, which cause Ψ and $\tilde{\Phi}$ not to be in $C^1(\Omega)$ with Ω being a bounded domain on which NMPBE is defined, we further express these two PDE systems in variational weak forms (see (11) and (14)). Consequently, we can use some standard variational techniques to carry out the analysis of NMPBE.

Following this approach, we proved that the linear nonlocal interface problem of Ψ has a unique solution in our previous work [41, Theorem 5.1]. However, we did not show that Ψ is bounded on the whole domain Ω since standard variational techniques do not work in the proof of a bounded solution. Such boundedness is required in our analysis of the nonlinear nonlocal interface problem that defines $\tilde{\Phi}$. Hence, a new analysis of Ψ becomes necessary.

In this paper, we obtain a new analysis of the linear nonlocal interface problem of Ψ (see Theorem 1). During the analysis, we present a new proof of the continuity and coercivity of a bilinear form defined in (12) (see Lemma 1), which plays a fundamental role in our analysis. As shown in the proof of Theorem 1, we also use Simader's approach [34] to overcome the difficulty that arises from estimating the boundedness of Ψ.

Finally, we use Schauder's fixed point arguments to prove that the nonlocal nonlinear interface problem of $\tilde{\Phi}$ has a solution (see Theorem 2). There are several versions of Schauder's fixed point theorem (see [13, p. 502] and [43, Theorem 2.A and Definition 2.9] for example). In our analysis, we used the original Schauder theorem as stated in the review article [17]. Via the solution decomposition, it implies the solution existence and uniqueness of NMPBE. Furthermore, by standard Banach fixed point arguments, we prove that the solution is unique under some conditions (see Theorem 3).

The remaining part of the paper is organized as follows. In Section 2, we define the NMPBE model and its solution decomposition. In Section 3, we describe the variational reformulations for both Ψ and $\tilde{\Phi}$. In Section 4, we prove the solution existence and uniqueness for the linear and nonlinear variational problems that define Ψ and $\tilde{\Phi}$.

2 The nonlocal modified Poisson-Boltzmann equation

Let D_p, D_s, and Γ be a protein region, a solvent region, and an interface between D_p and D_s, respectively. For a bounded domain Ω, we assume that $D_p \subset \Omega$, D_p is surrounded by D_s, and

$$\Omega = D_p \cup D_s \cup \Gamma,$$

where D_p hosts a protein molecule (or other biomolecules) with n_p atomic partial charge magnitudes $\{z_j\}_{j=1}^{n_p}$ at the atom positions $\{\mathbf{r}_j\}_{j=1}^{n_p}$, and D_s contains a symmetric 1:1 ionic solvent (e.g., a salt solution containing sodium (N_a^+) and chloride (Cl^-) ions), which is commonly used in application. A boundary value function, g, is assumed given on the boundary $\partial\Omega$ of Ω. Based on the implicit solvent approach [26, 35, 36, 37, 40, 41], both D_p and D_s are treated as dielectric continuum media with two different dielectric constants ϵ_p and ϵ_s satisfying $\epsilon_p < \epsilon_s$.

A nonlinear and nonlocal dielectric continuum model, called the nonlocal modified Poisson-Boltzmann equation (NMPBE), has been proposed in [39] for computing electrostatics of an ionic solvated protein. It is defined in a dimensionless form as follows:

$$\begin{cases} -\epsilon_p \Delta u(\mathbf{r}) = \dfrac{10^{10} e_c^2}{\epsilon_0 k_B T} \displaystyle\sum_{j=1}^{n_p} z_j \delta_{\mathbf{r}_j}, & \mathbf{r} \in D_p, \\ -\epsilon_\infty \Delta u(\mathbf{r}) + \dfrac{\epsilon_s - \epsilon_\infty}{\lambda^2}\big[u(\mathbf{r}) - (u * Q_\lambda)(\mathbf{r})\big] + \kappa^2 \sinh(u) = 0, & \mathbf{r} \in D_s, \\ u(\mathbf{s}^-) = u(\mathbf{s}^+), & \mathbf{s} \in \Gamma, \\ \epsilon_p \frac{\partial u(\mathbf{s}^-)}{\partial \mathbf{n}(\mathbf{s})} = \epsilon_\infty \frac{\partial u(\mathbf{s}^+)}{\partial \mathbf{n}(\mathbf{s})} + (\epsilon_s - \epsilon_\infty) \frac{\partial (u * Q_\lambda)(\mathbf{s})}{\partial \mathbf{n}(\mathbf{s})}, & \mathbf{s} \in \Gamma, \\ u(\mathbf{s}) = g(\mathbf{s}), & \mathbf{s} \in \partial\Omega, \end{cases} \tag{1}$$

where ϵ_0 is the permittivity constant for the vacuum, e_c is the elementary charge, ϵ_∞ is a dielectric constant for water in the limit of high frequency satisfying $\epsilon_s > \epsilon_\infty$, k_B is the Boltzmann constant, T is the absolute temperature, $\delta_{\mathbf{r}_j}$ is the Dirac delta distribution [29] with singularity at $\mathbf{r}_j$, $\mathbf{n}(\mathbf{s})$ denotes the unit outward normal vector of D_p, $\frac{\partial u(\mathbf{s})}{\partial \mathbf{n}(\mathbf{s})} = \nabla u(\mathbf{s}) \cdot \mathbf{n}(\mathbf{s})$, the expressions for κ, $u(\mathbf{s}^\pm)$, and $\frac{\partial u(\mathbf{s}^\pm)}{\partial \mathbf{n}(\mathbf{s})}$ are given by

$$\kappa^2 = 2I_s \frac{10^{-17} N_A e_c^2}{\epsilon_0 k_B T}, \quad u(\mathbf{s}^\pm) = \lim_{t \to 0^+} u(\mathbf{s} \pm t\mathbf{n}), \quad \frac{\partial u(\mathbf{s}^\pm)}{\partial \mathbf{n}(\mathbf{s})} = \lim_{t \to 0^+} \frac{\partial u(\mathbf{s} \pm t\mathbf{n}(\mathbf{s}))}{\partial \mathbf{n}(\mathbf{s})},$$

and $u * Q_\lambda$ denotes the convolution of u with the kernel function Q_λ, which is defined by

$$(u * Q_\lambda)(\mathbf{r}) = \int_{\mathbb{R}^3} Q_\lambda(\mathbf{r} - \mathbf{r}') u(\mathbf{r}') \mathrm{d}\mathbf{r}'. \tag{2}$$

Here, I_s is an ionic solvent strength in moles per liter (e.g., $I_s = 0.1$), N_A denotes the Avogadro number, λ is a nonlocal parameter that characterizes the polarization correlations of water molecules, and Q_λ is defined by

$$Q_\lambda(\mathbf{r}) = \frac{1}{4\pi\lambda^2 |\mathbf{r}|} e^{-|\mathbf{r}|/\lambda}.$$

The dimensionless NMPBE model (1) is derived from the assumption that the size of protein region D_p is measured in angstroms (Å) while all the other physical quantities are given in the SI (Le Système International d'Unités) units. For reference, we list the values and units of the physical constants e_c, T, k_B, and N_A in Table 1.

Table 1: Parameters of the NMPBE model (1) in SI units

Constant	Value	Unit (abbr.)	Name
ϵ_0	$8.854187817 \times 10^{-12}$	Farad/Meter (F/m)	Vacuum permittivity
e_c	$1.602176565 \times 10^{-19}$	Coulomb (C)	Elementary charge
T	298.15	Kelvin (K)	Absolute temperature
k_B	$1.380648813 \times 10^{-23}$	Joule/Kelvin (J/K)	Boltzmann constant
N_A	$6.02214129 \times 10^{23}$	Number of ions/mole	Avogadro number

The solution u of (1) is also referred to as an electrostatic potential in units k_BT/e_c, from which we can regain the electrostatic potential Φ in volts by the formula

$$\Phi = \frac{k_BT}{e_c}u.$$

When the domain Ω is large enough, the boundary value function g can be simply set to zero. Such a selection is often used in calculation due to the fact that the solution u quickly goes to zero as $|\mathbf{r}| \to \infty$. A proper selection of λ may vary from 3 to 30 depending on applications as shown in the studies reported in [2, 18, 19, 24, 33, 39] for example.

Because of the Dirac delta distributions $\delta_{\mathbf{r}_j}$, the solution u of the NMPBE has singularity points at each atomic position $\mathbf{r}_j$, causing difficulties in the analysis of NMPBE. One effective way to overcome the difficulties is to separate the singular and smooth parts of u by a solution decomposition formula. In this paper, we use the solution decomposition from [39] to construct the solution u of NMPBE as a sum of three component functions in the form

$$u(\mathbf{r}) = \Psi(\mathbf{r}) + \tilde{\Phi}(\mathbf{r}) + G(\mathbf{r}), \qquad \mathbf{r} \in \Omega, \tag{3}$$

where G is given by

$$G(\mathbf{r}) = \frac{10^{10}e_c^2}{4\pi\epsilon_p\epsilon_0 k_BT}\sum_{j=1}^{n_p}\frac{z_j}{|\mathbf{r}-\mathbf{r}_j|}, \tag{4}$$

which collects all the singular points $\mathbf{r} = \mathbf{r}_j$ for $j = 1, 2, \ldots, n_p$, Ψ is a solution of the linear nonlocal interface problem:

$$\begin{cases} \Delta\Psi(\mathbf{r}) = 0, & \mathbf{r} \in D_p, \\ -\epsilon_\infty\Delta\Psi + \dfrac{\epsilon_s-\epsilon_\infty}{\lambda^2}\big(\Psi - \Psi * Q_\lambda\big) = -\dfrac{\epsilon_s-\epsilon_\infty}{\lambda^2}\big(G - G * Q_\lambda\big), & \mathbf{r} \in D_s, \\ \Psi(\mathbf{s}^-) = \Psi(\mathbf{s}^+), & \mathbf{s} \in \Gamma, \\ \epsilon_p\dfrac{\partial\Psi(\mathbf{s}^-)}{\partial\mathbf{n}(\mathbf{s})} - \epsilon_\infty\dfrac{\partial\Psi(\mathbf{s}^+)}{\partial\mathbf{n}(\mathbf{s})} = (\epsilon_s-\epsilon_\infty)\dfrac{\partial(\Psi*Q_\lambda)(\mathbf{s})}{\partial\mathbf{n}(\mathbf{s})} + g_\Gamma(\mathbf{s}), & \mathbf{s} \in \Gamma, \\ \Psi(\mathbf{s}) = g(\mathbf{s}) - G(\mathbf{s}), & \mathbf{s} \in \partial\Omega, \end{cases} \tag{5}$$

and $\tilde{\Phi}$ is the solution of a nonlocal and nonlinear interface problem:

$$\begin{cases} \Delta\tilde{\Phi}(\mathbf{r}) = 0, & \mathbf{r} \in D_p, \\ -\epsilon_\infty \Delta\tilde{\Phi} + \dfrac{\epsilon_s - \epsilon_\infty}{\lambda^2}\left(\tilde{\Phi} - \tilde{\Phi} * Q_\lambda\right) + \kappa^2 \sinh(\tilde{\Phi} + \Psi + G) = 0, & \mathbf{r} \in D_s, \\ \tilde{\Phi}(\mathbf{s}^-) = \tilde{\Phi}(\mathbf{s}^+), & \mathbf{s} \in \Gamma, \\ \epsilon_p \dfrac{\partial\tilde{\Phi}(\mathbf{s}^-)}{\partial\mathbf{n}(\mathbf{s})} - \epsilon_\infty \dfrac{\partial\tilde{\Phi}(\mathbf{s}^+)}{\partial\mathbf{n}(\mathbf{s})} = (\epsilon_s - \epsilon_\infty)\dfrac{\partial(\tilde{\Phi} * Q_\lambda)(\mathbf{s})}{\partial\mathbf{n}(\mathbf{s})}, & \mathbf{s} \in \Gamma, \\ \tilde{\Phi}(\mathbf{s}) = 0, & \mathbf{s} \in \partial\Omega. \end{cases} \tag{6}$$

Here $g_\Gamma(\mathbf{s})$ is given by

$$g_\Gamma(\mathbf{s}) = (\epsilon_s - \epsilon_\infty)\frac{\partial(G * Q_\lambda)(\mathbf{s})}{\partial\mathbf{n}(\mathbf{s})} + (\epsilon_\infty - \epsilon_p)\frac{\partial G(\mathbf{s})}{\partial\mathbf{n}(\mathbf{s})}. \tag{7}$$

Clearly, G is smooth in D_s. With [42, Corollary A.1, p. 192], we can find an analytical expression for the convolution $\hat{G} = G * Q_\lambda$ as follows:

$$\hat{G}(\mathbf{r}) = \frac{10^{10} e_c^2}{4\pi\epsilon_p\epsilon_0 k_B T} \sum_{j=1}^{n_p} z_j \frac{1 - e^{-|\mathbf{r}-\mathbf{r}_j|/\lambda}}{|\mathbf{r} - \mathbf{r}_j|}, \tag{8}$$

from which follows an analytical expression of $\nabla\hat{G}$ and that both $\hat{G}$ and $\nabla\hat{G}$ are continuous in D_s. Thus, from the equations of (5) and (6) we can claim that both Ψ and $\tilde{\Phi}$ are twice continuously differentiable in D_p and D_s, respectively [16]. Hence, the interface problems (5) and (6) are well defined. In other words, the differential form (1) of NMPBE has been well redefined via the solution decomposition formula (3).

Clearly, setting $\epsilon_\infty = \epsilon_s$ immediately reduces the NMPBE model (1) to the classic PBE model:

$$\begin{cases} -\epsilon_p \Delta u(\mathbf{r}) = \dfrac{10^{10} e_c^2}{\epsilon_0 k_B T} \displaystyle\sum_{j=1}^{n_p} z_j \delta_{\mathbf{r}_j}, & \mathbf{r} \in D_p, \\ -\epsilon_s \Delta u(\mathbf{r}) + \kappa^2 \sinh(u) = 0, & \mathbf{r} \in D_s, \\ u(\mathbf{s}^-) = u(\mathbf{s}^+), \quad \epsilon_p \dfrac{\partial u(\mathbf{s}^-)}{\partial\mathbf{n}(\mathbf{s})} = \epsilon_s \dfrac{\partial u(\mathbf{s}^+)}{\partial\mathbf{n}(\mathbf{s})}, & \mathbf{s} \in \Gamma, \\ u(\mathbf{s}) = g(\mathbf{s}), & \mathbf{s} \in \partial\Omega. \end{cases} \tag{9}$$

Correspondingly, the solution decomposition of PBE given in [38] can be derived from the solution decomposition of NMPBE by setting $\epsilon_\infty = \epsilon_s$. Hence, an analysis of NMPBE can contain the PBE analysis as a special case.

In the solution decomposition (3), we have set the boundary values of $\tilde{\Phi}$ to be zero for the purpose of simplifying the calculation and analysis. Because of this special setting, Ψ collects all the electrostatic potential contributions from the boundary $\partial\Omega$ and the interface Γ. Clearly, $\tilde{\Phi}$ can be regarded as the electrostatic potential caused by ionic charges from the ionic solvent while G is the potential induced by the atomic charges of the protein immersed in the solute region being the whole space $\mathbb{R}^3$.

3 Variational formulation of NMPBE

Due to the jump of the flux interface conditions, we cannot expect that Ψ and $\tilde{\Phi}$ are in $C^1(\Omega)$. Thus, it is necessary to reformulate their interface problems (5) and (6) into variational weak forms in order to analyze them.

Let u_1, u_2, $\hat{g}$, and $\hat{G}$ denote the convolutions of Ψ, $\tilde{\Phi}$, g, and G, respectively, with the kernel function Q_λ being given in (2). It is known (see [20, 21] for example) that Q_λ is a Yukawa-type kernel satisfying the equation

$$-\lambda^2 \Delta Q_\lambda(\mathbf{r}) + Q_\lambda(\mathbf{r}) = \delta(\mathbf{r}), \quad \mathbf{r} \in \mathbb{R}^3,$$

where $\delta(\mathbf{r})$ denotes the Dirac-delta distribution at the origin. From the above equation we can easily find that u_1 and u_2 satisfy the equations

$$-\lambda^2 \Delta u_1(\mathbf{r}) + u_1(\mathbf{r}) - \Psi(\mathbf{r}) = 0, \quad -\lambda^2 \Delta u_2(\mathbf{r}) + u_2(\mathbf{r}) - \tilde{\Phi}(\mathbf{r}) = 0, \quad \mathbf{r} \in \mathbb{R}^3. \tag{10}$$

Let $H^1(\Omega)$ and $H_0^1(\Omega)$ denote the usual Sobolev function spaces, and set

$$\underset{\sim}{\phi}_1 = (\Psi, u_1), \quad \underset{\sim}{\phi}_2 = (\tilde{\Phi}, u_2), \quad \underset{\sim}{v} = (v_1, v_2), \quad \mathcal{V} = H_0^1(\Omega) \times H_0^1(\Omega).$$

Following what was done in [41], we can use (10) to obtain a variational weak form of the linear interface problem (5) as follows:

Find $\underset{\sim}{\phi}_1 \in H^1(\Omega) \times H^1(\Omega)$ satisfying $\Psi(\mathbf{s}) = g(\mathbf{s}) - G(\mathbf{s})$ and $u_1(\mathbf{s}) = \hat{g}(\mathbf{s}) - \hat{G}(\mathbf{s})$ for all $\mathbf{s} \in \partial\Omega$ such that

$$a(\underset{\sim}{\phi}_1, \underset{\sim}{v}) = \ell_1(\underset{\sim}{v}) \qquad \forall \underset{\sim}{v} \in \mathcal{V}, \tag{11}$$

where $a(\underset{\sim}{w}, \underset{\sim}{v})$ with $\underset{\sim}{w} = (w_1, w_2)$ is defined by

$$\begin{aligned} a(\underset{\sim}{w}, \underset{\sim}{v}) =& \epsilon_p \int_{D_p} \nabla w_1(\mathbf{r}) \cdot \nabla v_1(\mathbf{r}) \mathrm{d}\mathbf{r} + \epsilon_\infty \int_{D_s} \nabla w_1(\mathbf{r}) \cdot \nabla v_1(\mathbf{r}) \mathrm{d}\mathbf{r} \\ &+ (\epsilon_s - \epsilon_\infty) \int_{D_s} \nabla w_2(\mathbf{r}) \cdot \nabla v_1(\mathbf{r}) \mathrm{d}\mathbf{r} \\ &+ \lambda^2 \int_\Omega \nabla w_2(\mathbf{r}) \cdot \nabla v_2(\mathbf{r}) \mathrm{d}\mathbf{r} + \int_\Omega \left[w_2(\mathbf{r}) - w_1(\mathbf{r}) \right] v_2(\mathbf{r}) \mathrm{d}\mathbf{r}, \end{aligned} \tag{12}$$

and $\ell_1(\underset{\sim}{v})$ is defined by

$$\ell_1(\underset{\sim}{v}) = (\epsilon_\infty - \epsilon_s) \int_{D_s} \nabla \hat{G}(\mathbf{r}) \cdot \nabla v_1(\mathbf{r}) \mathrm{d}\mathbf{r} + (\epsilon_p - \epsilon_\infty) \int_{D_s} \nabla G(\mathbf{r}) \cdot \nabla v_1(\mathbf{r}) \mathrm{d}\mathbf{r}. \tag{13}$$

Similarly, the nonlinear interface problem (6) can be formulated as the following nonlinear variational problem: Find $\underset{\sim}{\phi}_2 \in \mathcal{V}$ such that

$$a(\underset{\sim}{\phi}_2, \underset{\sim}{v}) + \kappa^2 \int_{D_s} \sinh(\tilde{\Phi} + \Psi + G) v_1(\mathbf{r}) \, d\mathbf{r} = 0 \quad \forall \underset{\sim}{v} \in \mathcal{V}. \tag{14}$$

Introducing extra unknown functions u_1 and u_2 avoids the difficulties that may be caused by the convolution terms of NMPBE. The above two variational problems do not contain any convolution term, but the bilinear functional form $a(\cdot, \cdot)$ has become unsymmetric.

4 Solution existence and uniqueness of NMPBE

The analysis of NMPBE now can be done through analyzing the two variational problems given in (11) and (14). In [41, Theorem 5.1] it has been shown that (11) has a unique solution. But, as required by our analysis of the nonlinear variational problem (14), we have to estimate the boundedness of Ψ in the whole domain Ω. To do so, in this section, we present a new analysis of the linear variational problem (11) for Ψ. We then analyze the nonlinear variational problem (14) to prove the existence and uniqueness of $\tilde{\Phi}$.

We first show that the bilinear form $a(\cdot,\cdot)$ is bounded and coercive in Lemma 1.

Lemma 1 *Let $a(\cdot,\cdot)$ be a bilinear form defined in (12). If the parameter λ is sufficiently large, then there exist constants $C_1 > 0$ and $C_2 > 0$ such that*

$$|a(\underset{\sim}{w},\underset{\sim}{v})| \le C_1\|\underset{\sim}{w}\|_{H^1(\Omega)}\|\underset{\sim}{v}\|_{H^1(\Omega)} \quad \text{and} \quad |a(\underset{\sim}{v},\underset{\sim}{v})| \ge C_2\|\underset{\sim}{v}\|^2_{H^1(\Omega)} \quad \forall \underset{\sim}{w},\underset{\sim}{v} \in \mathcal{V}, \tag{15}$$

where the norm $\|\underset{\sim}{v}\|_{H^1(\Omega)}$ of $\mathcal{V}$ is defined by

$$\|\underset{\sim}{v}\|_{H^1(\Omega)} = \sqrt{\|v_1\|^2_{H^1(\Omega)} + \|v_2\|^2_{H^1(\Omega)}} \quad \text{for } \underset{\sim}{v} = (v_1, v_2) \in \mathcal{V}.$$

Proof. Set $\underset{\sim}{w} = (w_1, w_2)$ and $\underset{\sim}{v} = (v_1, v_2)$. For clarity, we set

$$a(\underset{\sim}{w},\underset{\sim}{v}) = a_0(\underset{\sim}{w},\underset{\sim}{v}) + a_1(\underset{\sim}{w},\underset{\sim}{v}),$$

where $a_0(\underset{\sim}{w},\underset{\sim}{v})$ and $a_1(\underset{\sim}{w},\underset{\sim}{v})$ are defined by

$$a_0(\underset{\sim}{w},\underset{\sim}{v}) = \int_\Omega \left(\epsilon(\mathbf{r})\nabla w_1 \cdot \nabla v_1 + \lambda^2 \nabla w_2 \cdot \nabla v_2 + w_2 v_2\right) d\mathbf{r},$$

and

$$a_1(\underset{\sim}{w},\underset{\sim}{v}) = c_1 \int_{D_s} \nabla w_2 \cdot \nabla v_1 \, d\mathbf{r} - \int_\Omega w_1 v_2 \, d\mathbf{r}.$$

Here, $c_1 = \epsilon_s - \epsilon_\infty$, and ϵ is defined by

$$\epsilon(\mathbf{r}) = \begin{cases} \epsilon_p, & \mathbf{r} \in D_p, \\ \epsilon_\infty, & \mathbf{r} \in D_s. \end{cases}$$

Clearly, a_0 is continuous on $\mathcal{V}$. The continuity of a_1 follows from

$$\begin{aligned} |a_1(\underset{\sim}{w},\underset{\sim}{v})| &\le \|w_1\|_{L^2(\Omega)}\|v_2\|_{L^2(\Omega)} + c_1\|\nabla w_2\|_{L^2(\Omega)}\|\nabla v_1\|_{L^2(\Omega)} \\ &\le \max\{1, c_1\}\|\underset{\sim}{w}\|_{H^1(\Omega)}\|\underset{\sim}{v}\|_{H^1(\Omega)}. \end{aligned}$$

This completes the proof of the continuity of $a(\cdot,\cdot)$ on $\mathcal{V}$.

To show the coercivity of a on $\mathcal{V}$, we first use Poincaré's inequality to get that

$$a_0(\underset{\sim}{v},\underset{\sim}{v}) \geq c_0\Big(\epsilon_{\min}\|v_1\|^2_{H^1(\Omega)} + \lambda^2\|v_2\|^2_{H^1(\Omega)}\Big) \qquad \forall \underset{\sim}{v} \in \mathcal{V},$$

where c_0 is the constant in Poincaré's inequality, and

$$\epsilon_{\min} = \min\{\epsilon_p, \epsilon_\infty\}.$$

From the Cauchy-Schwarz inequality it is known that

$$\left|\int_{D_s} \nabla v_1 \cdot \nabla v_2 \, d\mathbf{r}\right| \leq \frac{1}{2}\left(\delta_1\|v_1\|^2_{H^1(\Omega)} + \frac{1}{\delta_1}\|v_2\|^2_{H^1(\Omega)}\right) \quad \text{for any } \delta_1 > 0,$$

and

$$\left|\int_{\Omega} v_1 v_2 \, d\mathbf{r}\right| \leq \frac{1}{2}\left(\delta_2\|v_1\|^2_{H^1(\Omega)} + \frac{1}{\delta_2}\|v_2\|^2_{H^1(\Omega)}\right) \quad \text{for any } \delta_2 > 0.$$

Using the above inequalities with $\delta_1 = c_0\epsilon_{\min}/(\epsilon_s - \epsilon_\infty)$ and $\delta_2 = c_0\epsilon_{\min}/2$, we get

$$\begin{aligned}
&a(\underset{\sim}{v},\underset{\sim}{v}) = a_0(\underset{\sim}{v},\underset{\sim}{v}) + a_1(\underset{\sim}{v},\underset{\sim}{v}) \\
\geq&\Big(c_0\epsilon_{\min} - \frac{\delta_2}{2} - \frac{\delta_1(\epsilon_s-\epsilon_\infty)}{2}\Big)\|v_1\|^2_{H^1(\Omega)} + \Big(c_0\lambda^2 - \frac{1}{2\delta_2} - \frac{(\epsilon_s-\epsilon_\infty)}{2\delta_1}\Big)\|v_2\|^2_{H^1(\Omega)} \\
=&c_0\Big(\frac{\epsilon_{\min}}{4}\|v_1\|^2_{H^1(\Omega)} + \alpha_0\|v_2\|^2_{H^1(\Omega)}\Big) \\
\geq&c_0\min\left\{\frac{\epsilon_{\min}}{4}, \alpha_0\right\}\|\underset{\sim}{v}\|^2_{H^1(\Omega)} \qquad\qquad \forall \underset{\sim}{v} \in \mathcal{V},
\end{aligned}$$

where

$$\alpha_0 = \frac{2c_0^2\epsilon_{\min}\lambda^2 - (\epsilon_s-\epsilon_\infty)^2 - 2}{2c_0^2\epsilon_{\min}} = \lambda^2 - \frac{(\epsilon_s-\epsilon_\infty)^2+2}{2c_0^2\epsilon_{\min}} > 0 \tag{16}$$

provided that λ is large enough. Setting

$$\alpha_a = c_0\min\left\{\frac{\epsilon_{\min}}{4}, \alpha_0\right\}, \tag{17}$$

we conclude that

$$a(\underset{\sim}{v},\underset{\sim}{v}) \geq \alpha_a\|\underset{\sim}{v}\|^2_{H^1(\Omega)} \qquad \forall \underset{\sim}{v} \in \mathcal{V}, \tag{18}$$

and this completes the proof of the coercivity of a on $\mathcal{V}$. **QED**

We now present our analysis of the linear variational problem (11) in the following theorem.

Theorem 1 *If the parameter λ is sufficiently large, then the linear variational problem (11) has a unique solution. Moreover, for a Lipschitz continuous interface Γ, the solution Ψ satisfies*

$$\|\Psi\|_{L^\infty(\Omega)} \leq C\|\Psi\|_{W^1_p(\Omega)} < \infty \quad \textit{for } p > 3. \tag{19}$$

Proof. The boundedness of the linear functional ℓ_1 of (13) has been shown in the proof of [41, Theorem 5.1]. Thus, Lemma 1 and the Lax-Milgram Theorem [6, Theorem 2.7.7] imply the first part of Theorem 1.

To prove the second part of Theorem 1, we can write (5) as

$$\begin{cases} \Delta\Psi(\mathbf{r}) = 0, & \mathbf{r} \in D_p, \\ -\epsilon_\infty \Delta\Psi(\mathbf{r}) + \dfrac{\epsilon_s - \epsilon_\infty}{\lambda^2}\Psi(\mathbf{r}) = f(\mathbf{r}), & \mathbf{r} \in D_s, \\ \Psi(\mathbf{s}^-) = \Psi(\mathbf{s}^+), \quad \epsilon_p \dfrac{\partial\Psi(\mathbf{s}^-)}{\partial\mathbf{n}(\mathbf{s})} - \epsilon_\infty \dfrac{\partial\Psi(\mathbf{s}^+)}{\partial\mathbf{n}(\mathbf{s})} = b(\mathbf{s}), & \mathbf{s} \in \Gamma, \\ \Psi(\mathbf{s}) = g(\mathbf{s}) - G(\mathbf{s}), & \mathbf{s} \in \partial\Omega, \end{cases} \tag{20}$$

where f and b are defined by

$$f(\mathbf{r}) = \frac{\epsilon_s - \epsilon_\infty}{\lambda^2}(\Psi * Q_\lambda)(\mathbf{r}) - \frac{\epsilon_s - \epsilon_\infty}{\lambda^2}(G - G * Q_\lambda)(\mathbf{r}),\ \mathbf{r} \in D_s,$$

and

$$b(\mathbf{s}) = (\epsilon_s - \epsilon_\infty)\frac{\partial(\Psi * Q_\lambda)(\mathbf{s})}{\partial\mathbf{n}(\mathbf{s})} + g_\Gamma(\mathbf{s}).$$

We set $f(\mathbf{r}) = 0$ for $\mathbf{r} \in D_p$. Since $\Psi \in H^1(\Omega)$, we have $f \in L^\infty(\Omega)$. Thus, (20) can be reformulated as the variational problem

$$\int_\Omega \epsilon(\mathbf{r})\nabla\Psi(\mathbf{r}) \cdot \nabla v(\mathbf{r})\, d\mathbf{r} = \mathcal{F}(v) \quad \forall v \in H_0^1(\Omega), \tag{21}$$

where $\mathcal{F}$ is the linear functional defined by

$$\mathcal{F}(v) = \int_\Omega f(\mathbf{r})v(\mathbf{r})\, d\mathbf{r} + \oint_\Gamma b(s)v(s)\, ds \quad \forall v \in H_0^1(\Omega). \tag{22}$$

If Γ is Lipschitz continuous, then D_p and D_s are both measurable sets, and $b \in L^\infty(\Gamma)$, so by the trace theorem, we have $\mathcal{F} \in \left(W_1^1(\Omega)\right)'$. Moreover, with [31, Theorem 2], we know that

$$\Psi \in W_p^{1+s}(\Omega) \quad \text{for } 2 \le p < \infty \text{ and } 0 \le s < 1/p. \tag{23}$$

Hence, Sobolev's inequality [23, p. 61] and (23) imply (19). This completes the proof. **QED**

We next consider the nonlinear variational problem (14).

When $\kappa = 0$, the unique solution to (14) is $\underset{\sim}{\phi}_2 = \mathbf{0}$. For $\kappa > 0$, the problem is complicated by the fact that the standard variational approach to existence does not guarantee bounded solutions. Thus we use Simader's approach [34] which allows us to conclude that for two positive integers p and q satisfying $1/p + 1/q = 1$,

$$\|\underset{\sim}{\phi}\|_{W_p^1(\Omega)} \le C_p \sup_{\underset{\sim}{v} \in \mathcal{V}} \frac{a(\underset{\sim}{\phi}, \underset{\sim}{v})}{\|\underset{\sim}{v}\|_{W_q^1(\Omega)}}. \tag{24}$$

We now utilize Shauder's fixed point arguments to prove the solution existence for the nonlinear variational problem (14). There are several versions of Schauder's fixed point theorem (see [13, p. 502] and [43, Theorem 2.A and Definition 2.9] for example). We will use the original Schauder theorem, which is succinctly stated in the review article [17] as

Schauder's fixed point theorem: *Let H be a convex and closed subset of a Banach space. Then any continuous and compact map $F : H \to H$ has a fixed point.*

Let $F(\underset{\sim}{w})$ with $\underset{\sim}{w} = (w_1, w_2)$ denote a linear functional defined by

$$\langle F(\underset{\sim}{w}), \underset{\sim}{v}\rangle = -\kappa^2 \int_{D_s} \sinh(w_1(\mathbf{r}) + \Psi(\mathbf{r}) + G(\mathbf{r}))\, v_1(\mathbf{r})\, d\mathbf{r} \quad \text{for } \underset{\sim}{v} = (v_1, v_2) \in \mathcal{V}. \tag{25}$$

We construct a mapping $T : L^\infty(\Omega) \times L^\infty(\Omega) \to W_p^1(\Omega) \times W_p^1(\Omega)$ by

$$T(\underset{\sim}{w}) = \underset{\sim}{z} \in W_p^1(\Omega) \times W_p^1(\Omega) \quad \forall \underset{\sim}{w} = (w_1, w_2) \in L^\infty(\Omega) \times L^\infty(\Omega), \tag{26}$$

where $\underset{\sim}{z} = (z_1, z_2)$ denotes a unique solution of the following variational problem:

$$a(\underset{\sim}{z}, \underset{\sim}{v}) = \langle F(\underset{\sim}{w}), \underset{\sim}{v}\rangle \quad \forall \underset{\sim}{v} \in \mathcal{V}. \tag{27}$$

Let $K = \|\Psi + G\|_{L^\infty(D_s)}$. Because of (19), it is easy to see that $0 < K < \infty$. Using this constant and Schauder's fixed point theorem, we obtain a proof of the solution existence of the nonlinear variational system (14) in the following theorem.

Theorem 2 *Suppose that $3 < p < \infty$ and $K = \|\Psi + G\|_{L^\infty(D_s)} < \infty$. Then there is a constant $c_p < \infty$ such that, if the constant κ satisfies*

$$\kappa \le \sqrt{K/(c_p \sinh(2K))}\,, \tag{28}$$

then the nonlinear variational system (14) has a solution, $\underset{\sim}{\phi}_2$, and

$$\|\underset{\sim}{\phi}_2\|_{W_p^1(\Omega)} \le K.$$

Proof. Since $w_1 \in L^\infty(D_s)$, we can show that $F(\underset{\sim}{w})$, which is defined in (25), is bounded as follows:

$$|\langle F(\underset{\sim}{w}), \underset{\sim}{v}\rangle| \le \kappa^2 \sinh(2K)\|v_1\|_{L^1(D_s)} \le C\|\underset{\sim}{v}\|_{H^1(\Omega)} \quad \forall \underset{\sim}{v} \in \mathcal{V}. \tag{29}$$

Thus, from Lemma 1 and the Lax-Milgram theorem, (29) implies the solution existence and uniqueness of (27). Hence, the mapping T is well defined.

Moreover, (24) and (29) imply

$$\begin{aligned}\|\underset{\sim}{\phi}_2\|_{W_p^1(\Omega)} &\le C_p \sup_{\underset{\sim}{v}\in\mathcal{V}} \frac{\langle F(\phi_2), \underset{\sim}{v}\rangle}{\|\underset{\sim}{v}\|_{W_q^1(\Omega)}} \\ &\le C_p\kappa^2 \sinh(2K) \sup_{\underset{\sim}{v}\in\mathcal{V}} \frac{\|\underset{\sim}{v}\|_{L^1(D_s)}}{\|\underset{\sim}{v}\|_{W_q^1(\Omega)}} \\ &\le C_p\kappa^2 \sinh(2K)|D_s|^{1/p}.\end{aligned}$$

Finally, Sobolev's inequality implies that

$$\|\underset{\sim}{\phi}_2\|_{L^\infty(\Omega)} \le c_S\|\underset{\sim}{\phi}_2\|_{W_p^1(\Omega)} \le c_p \sinh(2K)\kappa^2 \le K$$

provided that

$$p > 3, \qquad \text{and} \qquad \kappa \le \sqrt{K/(c_p \sinh(2K))}.$$

Here $c_p = c_S C_p |D_s|^{1/p}$.

Since $0 < K < \infty$, we construct a ball, B_K, of radius K in $L^\infty(\Omega) \times L^\infty(\Omega)$ by

$$B_K = \{\underset{\sim}{w} = (w_1, w_2) \mid w_1, w_2 \in L^\infty(\Omega),\ \|\underset{\sim}{w}\|_{L^\infty(\Omega)} < K\},$$

and another bounded set, B'_K, in $W_p^1(\Omega) \times W_p^1(\Omega)$ by

$$B'_K = \{\underset{\sim}{z} = (z_1, z_2) \mid z_1, z_2 \in W_p^1(\Omega),\ \|\underset{\sim}{z}\|_{W_p^1(\Omega)} < C_p|D_s|^{1/p}K\}.$$

We know that T maps B_K into $B_K \cap B'_K$ for any $p > 3$. For such $p > 3$, Rellich's Theorem [13, p. 272] implies that the closure of the latter set in $L^\infty(\Omega)$ is compact. This proves that T is a compact mapping. Clearly, B_K is a convex and closed subset of the Banach space $L^\infty(\Omega) \times L^\infty(\Omega)$. Thus, Schauder's fixed point theorem implies that T has a fixed point, $\underset{\sim}{\phi}_2$, in B_K such that

$$\underset{\sim}{\phi}_2 = T(\underset{\sim}{\phi}_2).$$

QED

We next exhibit a solution by showing that T is a contraction provided that a different condition holds on κ, and moreover we prove that under this condition the nonlinear variational system (14) has a unique solution in the following theorem.

Theorem 3 *Let $K = \|\Psi + G\|_{L^\infty(D_s)}$, α_a be given in (17), and Λ_K be the Lipschitz constant for the function $s \to \sinh(s)$ on $[-2K, 2K]$. If the parameter κ of the nonlinear interface problem (6) satisfies*

$$\kappa < \sqrt{\alpha_a/\Lambda_K}\,, \tag{30}$$

then the nonlinear variational system (14) has a unique solution.

Proof. Using the mapping T defined in (26), we define a sequence, $\{\underset{\sim}{\phi}^{(n)}\}$, by

$$\underset{\sim}{\phi}^{(n)} = T\underset{\sim}{\phi}^{(n-1)}, \quad n = 1, 2, 3, \ldots,$$

where the initial guess $\underset{\sim}{\phi}^{(0)}$ is simply set as zero, and $\underset{\sim}{\phi}^{(n)} = (\tilde{\Phi}^{(n)}, u_2^{(n)})$ is defined by the linear variational system:

$$a(\underset{\sim}{\phi}^{(n)}, \underset{\sim}{v}) = -\kappa^2 \int_{D_s} \sinh(\tilde{\Phi}^{(n-1)} + \Psi + G) v_1 \, d\mathbf{r} \quad \forall \underset{\sim}{v} \in \mathcal{V}. \tag{31}$$

Similar to the second part of the proof of Theorem 2, we can claim that

$$\|\underset{\sim}{\phi}^{(n)}\|_{L^\infty(\Omega)} \le K \quad \text{for } n = 0, 1, 2, 3, \ldots. \tag{32}$$

We now consider the difference $e^{(n)} = \underset{\sim}{\phi}^{(n)} - \underset{\sim}{\phi}^{(n-1)}$. Let $U = \Psi + G$. Since

$$\left| \sinh(\tilde{\Phi}^{(n-2)}(\mathbf{r}) + U(\mathbf{r})) - \sinh(\tilde{\Phi}^{(n-1)}(\mathbf{r}) + U(\mathbf{r})) \right| \le \Lambda_K \left| \tilde{\Phi}^{(n-2)}(\mathbf{r}) - \tilde{\Phi}^{(n-1)}(\mathbf{r}) \right|,$$

for all $\mathbf{r}$, with (31), we have that for any $\underset{\sim}{v} \in \mathcal{V}$,

$$\begin{aligned} a(e^{(n)}, \underset{\sim}{v}) &= a(\underset{\sim}{\phi}^{(n)}, \underset{\sim}{v}) - a(\underset{\sim}{\phi}^{(n-1)}, \underset{\sim}{v}) \\ &= \kappa^2 \int_{D_s} (\sinh(\tilde{\Phi}^{(n-2)} + U) - \sinh(\tilde{\Phi}^{(n-1)} + U)) v_1 \, d\mathbf{r} \\ &\le \kappa^2 \Lambda_K \int_{D_s} |\tilde{\Phi}^{(n-2)} - \tilde{\Phi}^{(n-1)}| \, |v_1| \, d\mathbf{r} \\ &\le \kappa^2 \Lambda_K \|\underset{\sim}{\phi}^{(n-2)} - \underset{\sim}{\phi}^{(n-1)}\|_{L^2(\Omega)} \|\underset{\sim}{v}\|_{L^2(\Omega)} \\ &\le \kappa^2 \Lambda_K \|\underset{\sim}{\phi}^{(n-2)} - \underset{\sim}{\phi}^{(n-1)}\|_{H^1(\Omega)} \|\underset{\sim}{v}\|_{H^1(\Omega)} \\ &= \kappa^2 \Lambda_K \|e^{(n-1)}\|_{H^1(\Omega)} \|\underset{\sim}{v}\|, \end{aligned} \tag{33}$$

from which it follows that

$$\|e^{(n)}\|_{H^1(\Omega)} \le \kappa^2 \Lambda_K \alpha_a^{-1} \|e^{(n-1)}\|_{H^1(\Omega)}, \tag{34}$$

where α_a is defined in (17). Thus, under the condition (30), the mapping $\underset{\sim}{\phi}^{(n-1)} \to \underset{\sim}{\phi}^{(n)}$ is a contraction, and so the sequence $\{\underset{\sim}{\phi}^{(n)}\}$ converges to a solution of (14).

To show that (14) has a unique solution, we suppose that $\underset{\sim}{\phi}^1$ and $\underset{\sim}{\phi}^2$ are two solutions of (14) satisfying (32). A variant of (33) gives

$$\begin{aligned} a(\underset{\sim}{\phi}^1 - \underset{\sim}{\phi}^2, \underset{\sim}{v}) &= \kappa^2 \int_{D_s} (\sinh(\tilde{\Phi}^1 + U) - \sinh(\tilde{\Phi}^2 + U)) v_1 \, d\mathbf{r} \\ &\le \kappa^2 \Lambda_K \int_{D_s} |\tilde{\Phi}^1 - \tilde{\Phi}^2| \, |v_1| \, d\mathbf{r} \\ &\le \kappa^2 \Lambda_K \|\underset{\sim}{\phi}^1 - \underset{\sim}{\phi}^2\|_{L^2(\Omega)} \|\underset{\sim}{v}\|_{L^2(\Omega)} \\ &\le \kappa^2 \Lambda_K \|\underset{\sim}{\phi}^1 - \underset{\sim}{\phi}^2\|_{H^1(\Omega)} \|\underset{\sim}{v}\|_{H^1(\Omega)}. \end{aligned} \tag{35}$$

Using the coercivity (18), we have from (35) that

$$\|\underset{\sim}{\phi}^1 - \underset{\sim}{\phi}^2\|^2_{H^1(\Omega)} \leq \alpha_0^{-1} a(\underset{\sim}{\phi}^1 - \underset{\sim}{\phi}^2, \underset{\sim}{\phi}^1 - \underset{\sim}{\phi}^2) \leq \kappa^2 \Lambda_K \alpha_0^{-1} \|\underset{\sim}{\phi}^1 - \underset{\sim}{\phi}^2\|^2_{H^1(\Omega)} \tag{36}$$

which yields a contradiction

$$\|\underset{\sim}{\phi}^1 - \underset{\sim}{\phi}^2\|_{H^1(\Omega)} < \|\underset{\sim}{\phi}^1 - \underset{\sim}{\phi}^2\|_{H^1(\Omega)}$$

unless $\underset{\sim}{\phi}^1 = \underset{\sim}{\phi}^2$. **QED**

The condition (28) is less restrictive than (30). Asymptotically for large K, (28) means that we can take κ as large as $\kappa^2 \approx cKe^{-K}$, whereas (30) means that $\kappa^2 \approx ce^{-K}$ is the upper limit. In the former case, the solution may not be unique, but a continuation method could potentially be used to compute physically relevant solutions.

5 Conclusions

We have shown that the nonlocal modified PBE model is well posed. The proof involves only standard ideas, but there are two key difficulties to be addressed. One results from the Coulombic potential and the modeling of point charges via Dirac δ-functions, and the other is the unbounded nonlinear expression for the ionic correction. We handle the first by subtracting an analytical expression for the point charges in a vacuum and the second by a non-symmetric representation of the variational problem.

Acknowledgements

This work was partially supported by the National Science Foundation, USA, through grants DMS-1226259 and DMS-1226019.

References

[1] N. A. Baker, *Poisson-Boltzmann methods for biomolecular electrostatics*, Methods in enzymology, 383 (2003), pp. 94–118.

[2] M. Basilevsky and D. Parsons, *An advanced continuum medium model for treating solvation effects: Nonlocal electrostatics with a cavity*, Journal of Chemical Physics, 105 (1996), pp. 3734–3746.

[3] ——, *Nonlocal continuum solvation model with exponential susceptibility kernels*, Journal of Chemical Physics, 108 (1998), pp. 9107–9113.

[4] ——, *Nonlocal continuum solvation model with oscillating susceptibility kernels: A nonrigid cavity model*, Journal of Chemical Physics, 108 (1998), pp. 9114–9123.

[5] P. Bopp, A. Kornyshev, and G. Sutmann, *Static nonlocal dielectric function of liquid water*, Phys. Rev. Lett., 76 (1996), pp. 1280–1283.

[6] S. Brenner and L. Scott, *The Mathematical Theory of Finite Element Methods*, Springer-Verlag, New York, third ed., 2008.

[7] S. Buyukdagli and T. Ala-Nissila, *Microscopic formulation of nonlocal electrostatics in polar liquids embedding polarizable ions*, Phys. Rev. E, 87 (2013), p. 063201.

[8] L. Chen, M. J. Holst, and J. Xu, *The finite element approximation of the nonlinear Poisson-Boltzmann equation*, SIAM Journal on Numerical Analysis, 45 (2007), pp. 2298–2320.

[9] I. Chern, J. Liu, and W. Wang, *Accurate evaluation of electrostatics for macromolecules in solution*, Methods and Applications of Analysis, 10 (2003), pp. 309–328.

[10] J. Dai, I. Tsukerman, A. Rubinstein, and S. Sherman, *New computational models for electrostatics of macromolecules in solvents*, IEEE Transactions on Magnetics, 43 (2007), pp. 1217–1220.

[11] R. R. Dogonadze, E. Kálmán, A. A. Kornyshev, and J. Ulstrup, eds., *The Chemical Physics of Solvation. Part A: Theory of Solvation*, vol. 38 of Studies in Physical and Theoretical Chemistry, Elsevier Science Ltf, Amsterdam, October 1985.

[12] R. R. Dogonadze and A. A. Kornyshev, *Polar solvent structure in the theory of ionic solvation*, Journal of the Chemical Society, Faraday Transactions 2: Molecular and Chemical Physics, 70 (1974), pp. 1121–1132.

[13] L. Evans, *Partial Differential Equations*, vol. 19 of Graduate studies in mathematics, American Mathematical Society, 1998.

[14] F. Fogolari, A. Brigo, and H. Molinari, *The Poisson-Boltzmann equation for biomolecular electrostatics: A tool for structural biology*, J. Mol. Recognit., 15 (2002), pp. 377–392.

[15] C. García-García and D. Draper, *Electrostatic interactions in a peptide-RNA complex*, J. Mol. Biol., 331 (2003), pp. 75–88.

[16] D. Gilbert and N. S. Trudinger, *Elliptic Partial Differential Equations of Second Order*, Springer-Verlag, the 2nd ed., 1983.

[17] L. Górniewicz and D. Rozpłoch-Nowakowska, *On the Schauder fixed point theorem*, Banach Center Publications, 35 (1996), pp. 207–219.

[18] A. Hildebrandt, *Biomolecules in a structured solvent: A novel formulation of nonlocal electrostatics and its numerical solution*, PhD thesis, Saarlandes University, Saarbrücken, Germany, February 2005.

[19] A. Hildebrandt, R. Blossey, S. Rjasanow, O. Kohlbacher, and H. Lenhof, *Electrostatic potentials of proteins in water: A structured continuum approach*, Bioinformatics, 23 (2007), pp. e99–e103.

[20] A. Hildebrandt, R. Blossey, S. Rjasanow, O. Kohlbacher, and H.-P. Lenhof, *Novel formulation of nonlocal electrostatics*, Phys. Rev. Lett., 93 (2004), p. 108104.

[21] A. Kornyshev and A. Nitzan, *Effect of overscreeming on the localization of hydrated electrons*, Zeitschrift für Physikalische Chemie, 215 (2001), pp. 701–715.

[22] A. A. Kornyshev, A. I. Rubinshtein, and M. A. Vorotyntsev, *Model nonlocal electrostatics. I*, Journal of Physics C: Solid State Physics, 11 (1978), p. 3307.

[23] V. G. Mazỳa, *Sobolev spaces*, Springer, Berlin, 1985.

[24] S. Rick, *A reoptimization of the five-site water potential (TIP5P) for use with Ewald sums*, The Journal of Chemical Physics, 120 (2004), pp. 6085–6093.

[25] J. Rottler and B. Krayenhoff, *Numerical studies of nonlocal electrostatic effects on the sub-nanoscale*, Journal of Physics: Condensed Matter, 21 (2009), p. 255901.

[26] B. Roux and T. Simonson, *Implicit solvent models*, Biophys. Chem., 78 (1999), pp. 1–20.

[27] A. Rubinstein, R. Sabirianov, W. Mei, F. Namavar, and A. Khoynezhad, *Effect of the ordered interfacial water layer in protein complex formation: A nonlocal electrostatic approach*, Physical Review E, 82 (2010), p. 021915.

[28] A. Rubinstein and S. Sherman, *Influence of the solvent structure on the electrostatic interactions in proteins*, Biophysical Journal, 87 (2004), pp. 1544–1557.

[29] W. Rudin, *Functional Analysis*, McGraw-Hill, New York, 2nd ed., 1991.

[30] B. Sahin and B. Ralf, *Nonlocal and nonlinear electrostatics of a dipolar coulomb fluid*, Journal of Physics: Condensed Matter, 26 (2014), p. 285101.

[31] G. Savaré, *Regularity results for elliptic equations in Lipschitz domains*, Journal of Functional Analysis, 152 (1998), pp. 176–201.

[32] L. Scott, M. Boland, K. Rogale, and A. Fernández, *Continuum equations for dielectric response to macro-molecular assemblies at the nano scale*, Journal of Physics A: Math. Gen., 37 (2004), pp. 9791–9803.

[33] L. Ridgway Scott, Yi Jiang, and Xie Dexuan, *Comparison of a nonlocal dielectric model with a discontinuous model*, Research Report UC/CS TR-2015-06, Dept. Comp. Sci., Univ. Chicago, 2015.

[34] C. G. Simader, *On Dirichlet's boundary value problem*, Springer, 1972.

[35] Y. N. Vorobjev, *Advances in implicit models of water solvent to compute conformational free energy and molecular dynamics of proteins at constant pH*, Advances in Protein Chemistry and Structural Biology, 85 (2011), pp. 281–322.

[36] S. Weggler, V. Rutka, and A. Hildebrandt, *A new numerical method for nonlocal electrostatics in biomolecular simulations*, J. Comput. Phys., 229 (2010), pp. 4059 – 4074.

[37] G. Wilson, R. Chan, D. Davidson, and E. Whalley, *Dielectric properties of ices II, III, V, and VI*, Journal of Chemical Physics, 43 (1965), pp. 2384–2391.

[38] D. Xie, *New solution decomposition and minimization schemes for Poisson-Boltzmann equation in calculation of biomolecular electrostatics*, J. Comput. Phys., 275 (2014), pp. 294–309.

[39] D. Xie and Y. Jiang, *A nonlocal modified Poisson-Boltzmann equation and finite element solver for computing electrostatics of biomolecules.* Submitted, 2015.

[40] D. Xie, Y. Jiang, P. Brune, and L. Scott, *A fast solver for a nonlocal dielectric continuum model*, SIAM J. Sci. Comput., 34 (2012), pp. B107–B126.

[41] D. Xie, Y. Jiang, and L. Scott, *Efficient algorithms for a nonlocal dielectric model for protein in ionic solvent*, SIAM J. Sci. Comput., 38 (2013), pp. B1267–1284.

[42] D. Xie and H. Volkmer, *A modified nonlocal continuum electrostatic model for protein in water and its analytical solutions for ionic Born models*, Commun. Comput. Phys., 13 (2013), pp. 174–194.

[43] E. Zeidler, *Nonlinear Functional Analysis and its Applications I: Fixed-Point Theorems*, Springer Verlag, 1986.