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AN EFFECTIVE MINIMIZATION PROTOCOL FOR SOLVING A SIZE-MODIFIED POISSON-BOLTZMANN EQUATION FOR BIOMOLECULE IN IONIC SOLVENT

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Abstract. The size-modified Poisson-Boltzmann equation (SMPBE) has been developed to consider ionic size effects in the calculation of electrostatic potential energy, but its numerical solution for a biomolecule remains a challenging research issue. To address this challenge, in this paper, we propose a solution decomposition formula and then develop an effective minimization protocol for solving the nonlinear SMPBE model by using finite element approximation techniques. As an application, a particular SMPBE numerical algorithm is constructed and programmed as a finite element program package for a biomolecule (e.g., protein and DNA) in a symmetric 1:1 ionic solvent. We also construct a nonlinear SMPBE ball model with an analytical solution and use it for validation of our new SMPBE numerical algorithm and program package. Furthermore, numerical experiments are made on a central charged ball model to show some physical features captured by the SMPBE model. Finally, they are made for six biomolecules with different net charges to demonstrate the computer performance of our SMPBE finite element program package. Numerical results show that the SMPBE model can capture some physical properties of an ionic solvent more reasonably, and can be solved more efficiently than the classic PBE model. As an application of the SMPBE model, free solvation energies were calculated and compared to the case of the PBE model.

Key words. Poisson-Boltzmann equation, variational minimization, finite element method, implicit solvent, electrostatic potential.

1. Introduction

The Poisson-Boltzmann equation (PBE) has been widely applied to the study of protein docking, ion channel modeling, and rational drug design [6, 12, 13, 20]. Despite its success in many applications, it has been well known to have some drawbacks in the calculation of electrostatic free energy for a highly charged biomolecule immersed in an ionic solvent with a high salt concentration, since it neglects ionic size effects on the biomolecular electrostatic free energy. As an improvement of the PBE model, a size-modified PBE (SMPBE) model was proposed by simply assuming that all water molecules and ions occupy the same space of a cube with side length e Λ [1]. It was recently extended to a case of nonuniform ionic sizes [2, 16, 18, 21]. However, even for the simple SMPBE model, the study of numerical solutions was only limited to a small biological molecule in a monovalent ion solution [10] and a case of one spheric ball containing a central charge or a small molecule with three atoms in a salt solution so far [2, 5, 26]. How to solve the SMPBE model effectively and efficiently for a large biomolecule in an ionic solvent remains a challenging research issue in the fields of computational biology, computational mathematics, and high performance scientific computing.

To address such a challenge, in this paper, we propose a solution decomposition formula (see Theorem 2.1), which naturally splits the SMPBE solution u, into

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three component functions G, Ψ, and $\tilde{\Phi}$, respectively, according to the potential contributions from the biomolecular charges, the interface and boundary value conditions, and the ionic solvent charges. Since G collects all the singular points of u and is known in an analytical expression, the SMPBE numerical solution problem is remarkably simplified as the numerical solutions of one well defined nonlinear elliptic interface problem for $\tilde{\Phi}$ (see (5)) and one well defined linear elliptic interface problem for Ψ (see (6)). We then construct a nonlinear minimization problem and prove that this minimization problem has the same unique solution as the nonlinear interface problem so that $\tilde{\Phi}$ can be found through solving the minimization problem. In this way, we obtain an effective minimization protocol for solving the SMPBE model using finite element approximation techniques. As a result, it becomes possible for us to develop a global convergent iterative algorithm for solving the nonlinear SMPBE model. Note that setting a value of uniform size parameter Λ to be zero immediately reduces the SMPBE model to the classic PBE model. Hence, the SMPBE model contains the PBE model as a special case, and our work of this paper is an extension of our work on the classic PBE model [22, 23].

Different selections of linear and nonlinear iterative methods within our minimization protocol may result in different SMPBE numerical algorithms. As initial work, in this paper, we construct a particular SMPBE numerical algorithm for a biomolecule in a symmetric 1:1 ionic solvent by using a simple Newton minimization method. We then programmed this SMPBE algorithm as a finite element program package based on the FEniCS finite element library [17] and the molecular surface and volumetric mesh generation program package `GAMer` [24]. Our SMPBE program package is easy to use and portable on different computer systems because its main program is written in Python.

To verify our algorithm and program package, we construct a SMPBE ball model with an analytical solution (see (25)). We then solved it using our SMPBE program package. Numerical results validate our new SMPBE algorithm and program package, and show that a higher accuracy of the finite element solution can be achieved with a higher order of the finite element approximation.

We next made numerical experiments on a central charged ball immersed in the salt solution. Numerical results confirm that the SMPBE model can much better capture some physical features of ionic solvent than the classic PBE model.

Furthermore, we did numerical tests on six biomolecules with different net charges to demonstrate the computer performance of our new SMPBE program package. Although the SMPBE model is more complicated than the classic PBE model, our numerical results show that a SMPBE numerical solution could be found in less CPU time than the corresponding PBE numerical solution. For example, on one 2.4 GHz Intel Core i5 processor of a MacBook Pro, our SMPBE program package took only about 28 seconds for a biomolecule with 2124 atoms over a finite element mesh with 77,663 vertices; in contrast, the PBE program package took about 56 seconds for the corresponding PBE finite element solution [22].

Finally, as one important application, we calculated free solvation energies for the six biomolecules using the SMPBE program package and compared them with the ones calculated by our PBE program package [22]. Numerical results show that the PBE model always produced a smaller free solvation energy than the SMPBE model, and a value of the solvation energy becomes increasing when a larger value of Λ is used for the SMPBE model if Λ is treated as a purely scale parameter.