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FINITE VOLUME ELEMENT METHOD FOR PREDICTING ELECTROSTATICS OF A BIOMOLECULE IMMERSED IN AN IONIC SOLVENT

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Abstract. Poisson-Boltzmann equation (PBE) is a classic implicit continuum model to predict the electrostatic potentials of a solvated biomolecule. In this paper, we present a finite volume element method specific to the elliptic interface problem with a non-homogeneous flux condition for solving PBE and provide a follow-up analysis. The new PBE solver is fulfilled through both `Fortran` and `Python`, afterwards the local Poisson test model coupled with an analytical solution is adopted to well validate the program. Lastly, an application of the new solver to the prediction of solvation free energies of the proteins is made.

Key words. Poisson-Boltzmann equation, electrostatic free energy, finite volume element method, solvation free energy.

1. Introduction

The electrostatics referring to a protein immersed in an ionic solvent are important to recognize its biological structure and the various relevant functions [22, 26]. At present, one commonly-used mathematical model for predicting electrostatics is the Poisson-Boltzmann model, which has been employed in various applications such as protein docking, ion channel modeling, and rational drug design [21]. Up to now, the mathematical theory of Poisson-Boltzmann equation (PBE) and its variants have been well analyzed [14, 29] by considering an electrostatic free energy minimization problem subject to the Poisson dielectric model. Meanwhile, these models have been efficiently and accurately solved by finite element method (FEM) [1, 12, 15, 28], finite difference method [27, 38], boundary element method [19], and some mixed methods [2, 34, 35, 36]. Besides, to simulate the electrodiffusion in numerous biological processes, Poisson-Nernst-Planck equation (PNP) as well as its improved models [20, 23] have also been proposed and commonly used as well.

It is well-known that FEM is used to solve the interface problems of both PBE and PNP thanks to its flexibility of handling the complex interface. As alternatives, finite volume methods not only can deal with the complex interface very well, but also preserve the local conservation laws of some physical quantities such as mass and flux. Additionally, in comparison with FEM, its computational cost is relatively less while it aims at the explicit evolved equation with time. To authors' best knowledge, it only has been used so far to solve on Cartesian grids both PBE [10] and size-modified PBE [24] without explicitly considering the interface, and to predict the double layer forces between spherical colloidal particles [17], latter of which considered the Poisson equation without interface. Therefore, finite volume methods have never been used to solve PBE and its variants yet. The finite volume element method (FVEM, see e.g. [3, 11, 16, 33, 37]), one type of finite volume methods, has gained increasing attention recently. Owe to the same mesh

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and basis functions being used in the discretization process as that of FEM, FVEM possesses almost all the advantages of FEM such as flexibility to handle the complex interface and domain with arbitrary geometry. Meanwhile, the preservation of local conservation laws about certain physical quantities makes FVEM especially important for PNP [20]. As the first step of several potential subsequent works, we attempt to solve PBE via FVEM in this work.

By virtue of the decomposition scheme intended for isolating the singularities caused by the Dirac delta distributions, the solution u of PBE is splitted into three parts: solution G in an analytical expression, solution Ψ subject to a linear interface problem with a non-homogeneous flux condition on the interface, and solution $\tilde{\Phi}$ tied to a nonlinear interface problem. Through literature on finite volume methods, an elliptic equation with a non-homogenous flux condition on the interface has never been discussed yet. Our work is the first to propose a new technique to overcome the difficulties induced by the non-homogenous flux condition. For any vertices on the interface in an given unstructured mesh, we artificially separate their control volumes into pairs so that the interface lies on the common boundary of the two sub-control volumes. As a result, the non-homogeneous flux condition can be incorporated into the variational form through integration-by-part performed on those separated sub-control volumes.

Based on the proposed technique, we formulate a new finite volume element PBE solver and fulfill it in both `Python` and `Fortran`. The local Poisson test model owning an analytical solution in a series form involving Legendre polynomials is used to validate the new program. The tests show that applying our technique to deal with the non-homogeneous flux condition gives rise to the second-order convergence in L_2 norm and the first-order convergence in H^1 norm, which is exactly the same as FVEM has achieved [33]. As an application, the new solver is subsequently applied to predict the solvation free energies of some proteins. Meanwhile, the obtained energies are compared to the ones derived from the finite element PBE solver [28] engaging the same unstructured meshes. These numerical tests illustrate that the predicted solvation free energies are quite close to each other although different numerical methods are adopted.

The rest of the paper is organized as follows. A short review of PBE solution decomposition is given in Section 2. Section 3 is devoted to presenting our FVEM formulation specific to the regularized PBE. At the end of this section, a new algorithm for solving PBE is presented. We present an analysis of the FVEM for PBE in Section 4. The validation test on local Poisson test model as well as the application of the new solver in predicting the solvation free energy is conducted in Section 5.

2. Solution decomposition of the Poisson-Boltzmann model

Let Ω be a sufficiently large bounded domain of $\mathbb{R}^3$ (See Figure 1 for an illustration) satisfying

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

where D_p denotes a solute region hosting a protein molecule with n_p atoms, D_s denotes a solvent region, and Γ is the interface between D_p and D_s. Under the implicit solvent approach, both D_p and D_s are treated as continuum media with dielectric constants ϵ_p and ϵ_s, respectively. Then for a symmetric 1:1 ionic solvent (e.g., a salt solution with sodium (Na^+) and chloride (Cl^-) ions), the electrostatic potential u (in unit k_BT/e_c) can be predicted by the following boundary value