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An Adaptive, Finite Difference Solver for the Nonlinear Poisson-Boltzmann Equation with Applications to Biomolecular Computations

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Abstract. We present a solver for the Poisson-Boltzmann equation and demonstrate its applicability for biomolecular electrostatics computation. The solver uses a level set framework to represent sharp, complex interfaces in a simple and robust manner. It also uses non-graded, adaptive octree grids which, in comparison to uniform grids, drastically decrease memory usage and runtime without sacrificing accuracy. The basic solver was introduced in earlier works [16, 27], and here is extended to address biomolecular systems. First, a novel approach of calculating the solvent excluded and the solvent accessible surfaces is explained; this allows to accurately represent the location of the molecule's surface. Next, a hybrid finite difference/finite volume approach is presented for discretizing the nonlinear Poisson-Boltzmann equation and enforcing the jump boundary conditions at the interface. Since the interface is implicitly represented by a level set function, imposing the jump boundary conditions is straightforward and efficient.

AMS subject classifications: 92-08, 65N06, 65N08, 65N50, 92C05, 35F21

Key words: Poisson-Boltzmann, non-graded adaptive grid, octree data structure, level set, irregular domain, hybrid finite volume/finite difference.

1 Introduction

The Poisson-Boltzmann equation is useful for calculating important biomolecular quantities, such as pKa values and energies of binding [12]. However, solving this equation

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numerically has many challenges, the most significant of which are a) charge singularities, b) representing molecular surfaces, c) addressing exponential nonlinearities in the solution, and d) imposing the correct jump boundary condition. In this work, we present a solver that addresses some of the computational challenges in novel ways. First, we describe a simple and robust technique for implicitly representing biomolecular surfaces. Next, we demonstrate a novel discretization method for imposing the correct jump boundary conditions on the surface. Finally, we validate the solver and show its usefulness by calculating solvation free energies.

Since the pioneering work of Warwicker and Watson in the early 1980s [39], many different techniques for solving the Poisson-Boltzmann equation have been developed, most of which are based on finite difference, finite element, or boundary element methods. In this work, we do not intend to describe or compare them and refer the interested reader to [2,3,7,18,21] and the references therein for recent reviews.

An important characteristic of modern Poisson-Boltzmann solvers is the solver ability to use variable resolution. This allows to have coarse resolution where the solution is smooth and fine resolution where the solution varies rapidly. Indeed, one of the advantages of finite element methods over finite difference methods has been the robust adaptivity. Finite element methods are able to locally refine the computational mesh based on an error indicator, increasing resolution as needed, which enabled them to more efficiently address the exponential nonlinearity in the Poisson-Boltzmann equation [3,21]. Finite difference solvers can achieve similar results through the practice of focusing, in which the equation is solved on a coarse mesh, and the solution is used as a boundary condition for a finer mesh over an interesting subdomain [14].

Recent works have introduced adaptive finite difference methods that discretize the Poisson-Boltzmann equation on non-uniform grids. In [5], Boschitsch and Fenley introduced a first-order method that solves the nonlinear Poisson-Boltzmann equation on a graded octree mesh. In [27] and [16], Gibou and coworkers presented a second-order method for solving the Poisson-Boltzmann equation on a non-graded octree mesh. Neither use error estimates to refine the mesh, however. Instead, they refine the mesh based on distance from the molecular surface. The rational is based on the elliptic nature of the equation, which ensures that the solutions are smooth away from the interface.

Another difference between finite difference and finite element methods is that finite element methods ensure that cell edges align with interfaces. This is an appealing feature, as interfaces cutting through cells — as happens in finite difference schemes — complicate the discretization of boundary conditions. This property, however, comes at a price; creating a finite element mesh for a geometrically complicated domain, such as the surface of a protein, can be very expensive [8].

Finite difference methods, on the other hand, do not require the grid to conform to the boundary. As a result the grid generation, for uniform meshes, is trivial. However, since the grid does not conform to the boundary, special care must be taken to discretize the boundary conditions. This is specially important for biomolecular computations since one has to impose jump boundary conditions on complicated and, potentially, singular