Exploring an Alternative Method to Compute Protein Electrostatics

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Introduction

The electrostatic potential of proteins has been used to study protein stability, pH dependent properties, e.g. ionization state, steering of substrates in binding, and the influence of solvent in dynamics. Currently an analytic solution to calculate the forces from the electrostatic potential for proteins is not available making it difficult to use in molecular dynamic calculations. Several methods have been developed and optimized to use the Poisson Boltzmann equation in molecular dynamics calculations. One method that has not been examined is the use of Green's functions and the solving of surface integrals. This method has advantages over the currently preferred finite difference and finite element methods.

Hypothesis

Our hypothesis is that an accurate and efficient method to obtain the electrostatic potential and forces can be accomplished using a Green's function approach. The Green's function approach is a technique used to solve partial differential equations.

Specific Aims

The above hypothesis will be tested in the following specific aims:

1. Develop an algorithm that defines the surface of an arbitrarily shaped object. In this specific aim we will develop and algorithm, based on spherical harmonics, to define the surface of a protein.
2. Implement a Green's function approach to solve for the electrostatic potential and forces. Using the spherical harmonic representation of the protein surface we will solve for the electrostatic potential for the protein.

3. Implement the ACA algorithm. In this aim we will increase the efficiency of the Green's function approach by reducing the size of the problem using the ACA algorithm. Once this has been accomplished we will further optimize the solution by developing a parallel computing solution.
4. Compare the solutions to other Poisson-Boltzmann solvers. We will compare the accuracy and efficiency of our method to those currently used in the biophysics community, e.g. APBS, UHBD, CHARMM, and DelPhi.