

Fast Methods for Simulation of Biomolecule of Electrostatics

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Abstract—Biomolecular structure and interactions in aqueous environment are determined by a complicated interplay between physical and chemical forces including solvation, electrostatics, van der Waals forces, the hydrophobic effect and covalent bonding. Among them, electrostatics has been of particular interest due to its long-range nature and the tradeoff between desolvation and interaction effects [1]. In addition, electrostatic interactions play a significant role within a biomolecule as well as between biomolecules, making the balance between the two vital to the understanding of macromolecular systems. As a result, much effort has been devoted to accurate modeling and simulation of biomolecule electrostatics. One important application of this work is to compute the structure of electrostatic interactions for a biomolecule in an electrolyte solution, as well as the potential that the molecule generates in space. There are two valuable uses for these simulations. First, it provides a full picture of the electrostatic energetics of a biomolecular system, improving our understanding of how electrostatics contributes to stability, specificity, function, and molecular interaction [2]. Second, these simulations serve as a tool for molecular design, since electrostatic complementarity is an important feature of interacting molecules. Through examination of the electrostatics and potential field generated by a protein molecule, for example, it may be possible to suggest improvements to other proteins or drug molecules that interact with it, or perhaps even design new interacting molecules de novo [3].

There are two approaches in simulating a protein macromolecule in an aqueous solution with nonzero ionic strength. Discrete/atomistic approaches based on Monte-Carlo or molecular dynamics simulations treat the macromolecule and solvent explicitly at the atomic level. Therefore, an enormous number of solvent molecules are required to provide reasonable accuracy, especially when electric fields far away from macroscopic surface are of interest, leading to computational infeasibility. In this work, we adopt instead an approach based on a continuum description of the macromolecule and solvent. Although the continuum model of biomolecule electrostatics is widely used, the numerical techniques used to evaluate the model do not exploit fast solver approaches developed for analyzing integrated circuit interconnect. I will describe the formulation used for analyzing biomolecule electrostatics, and then derive an integral formulation of the problem that can be rapidly solved with precorrected-FFT method [4].

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