

## The Geometry Behind Numerical Solvers of the Poisson-Boltzmann Equation

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**Abstract.** Electrostatics interactions play a major role in the stabilization of biomolecules: as such, they remain a major focus of theoretical and computational studies in biophysics. Electrostatics in solution is strongly dependent on the nature of the solvent and on the ions it contains. While methods that treat the solvent and ions explicitly provide an accurate estimate of these interactions, they are usually computationally too demanding to study large macromolecular systems. Implicit solvent methods provide a viable alternative, especially those based on Poisson theory. The Poisson-Boltzmann equation (PBE) treats the system in a mean field approximation, providing reasonable estimates of electrostatics interactions in a solvent treated as continuum. In the first part of this paper, we review the theory behind the PBE, including recent improvement in which ions size and dipolar features of solvent molecules are taken into account explicitly. The PBE is a non linear second order differential equation with discontinuous coefficients, for which no analytical solution is available for large molecular systems. Many numerical solvers have been developed that solve a discretized version of the PBE on a mesh, either using finite difference, finite element, or boundary element methods. The accuracy of the solutions provided by these solvers highly depend on the geometry of their underlying meshes, as well as on the method used to embed the physical system on the mesh. In the second part of the paper, we describe a new geometric approach for generating unstructured tetrahedral meshes as well as simplifications of these meshes that are well fitted for solving the PBE equation using multigrid approaches.

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## 1 Introduction

Electrostatics interactions are central in physics, chemistry and biology: without them, molecules would not hold together. Understanding electrostatics is especially important in biology: biomolecules are usually considered as large polyelectrolytes, whose properties depend on their own charge distribution as well as on their interactions with surrounding charged neighbors. In the case of proteins for example, Kauzmann [1] foresaw the importance of electrostatics for stability, proposing that polar (charged) groups would either compensate for each other, or be solvated by water. Later, Perutz [2] confirmed these predictions based on information deduced from the first high resolution protein structures, and further emphasized the role of electrostatics in biomolecular interactions. Electrostatics is even more important for nucleic acids. RNA and DNA are polyanions that bind water and cations in order to acquire a three-dimensional structure. It is well known that in the absence of metal ions, RNA and DNA form most of their secondary structures, but only a fraction (if any) of their tertiary contacts [3]. Accurate theoretical and subsequent numerical treatments of electrostatics has therefore always been a major concern in structural biology.

Theoretical modeling of electrostatics interactions is deceptively simple and, as such, has been and remains the subject of development by both the physics and the scientific computing communities. As a first 'classical' approximation, the interaction between two charges can be described by Coulomb's law. When more than two charges interact, the total electrostatic energy of the system is derived as the sum of all pairwise Coulomb interactions (superposition principle). Applications of these simple principles imply that the positions of all charges are known. While this seems to be a simple requirement, it is unfortunately difficult to meet when modeling large molecular systems. This is mostly due to the inherent difficulties in accounting for the solvent that surrounds the molecules and the ions this solvent may contain. Explicit representation of the solvent provides an accurate treatment of electrostatics, but it increases the size of the system under study by orders of magnitude [4]. In addition, interactions involving solvent need to be averaged over relatively long time intervals before results become meaningful. As a response to these problems, there has been a continuous effort in the physics community to develop simplified models that are computationally tractable and that remain physically accurate. Most of these models include the solvent implicitly, reducing the solute-solvent interactions to their mean field characteristics, which are expressed as functions of the solute degrees of freedom alone. These approaches treat the solvent as a dielectric continuum and are therefore referred to as a continuum dielectric model. Many of these approaches use the Poisson-Boltzmann equation to describe the electrostatic potential of a system, and rely on numerical methods to solve this non linear elliptic equation. This paper is designed around two distinctive parts. Firstly, it provides an overview of the recent methodological developments in designing fast and accurate solvers of the Poisson-Boltzmann equation. We also cover recent theoretical models that modify the Poisson-Boltzmann equation to better represent the physics of the system under study.