QUANTIFYING ATOMIC POSITION UNCERTAINTY IN MOLECULAR ELECTROSTATICS WITH POISSON-BOLTZMANN AND BOUNDARY ELEMENTS

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Abstract. Electrostatic interactions are fundamental to molecular processes, structure, and function. Accurately modeling these interactions is essential for understanding molecular behavior. The Poisson-Boltzmann equation is a widely used tool to this end, applied to model scenarios where a dissolved solute is represented as a low dielectric region in an infinite solvent domain, containing Dirac deltas to represent partial charges. Traditional Poisson-Boltzmann calculations often assume structural rigidity, overlooking thermal fluctuations that significantly impact atomic positions. These fluctuations result in structural variations, introducing inherent uncertainty into solvation energy predictions.

We present a methodology that integrates the solution of the Poisson-Boltzmann equation with the boundary element method, with quasi-Monte Carlo sampling techniques to accommodate the dynamic nature of solute molecules in solution. This way, we quantify the uncertainty arising from these thermal fluctuations, providing a more realistic representation of solvation energies. We validate our approach using a large dataset of realistic molecules, leveraging from molecular dynamics simulations for benchmarking. Furthermore, we extend our method to estimate uncertainty in solvation energies for larger structures, like proteins.

Importantly, our research contributes to an open-source and FAIR (Findable, Accessible, Interoperable, Reusable) software infrastructure, promoting transparency, collaboration, and accessibility. This work enhances the accuracy of solvation energy calculations and underscores the importance of incorporating uncertainty quantification in molecular modeling.

Keywords: Poisson-Boltzmann, Uncertainty Quantification, Molecular Electrostatics, Boundary Element Method.

Mathematics Subject Classifications (2010): 92E10, 92C40, 45A05

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