Future-Proofing Fast Electrostatic Models for the Era of Massive Parallelism

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Molecular simulations of proteins and nanosystems continue to grow rapidly in scale, making computation speed a critical challenge despite exponentially increasing computational power (via massively parallel supercomputers and the rise of graphics processing units, GPUs). Implicit-solvent models represent a valuable and widely used way to dramatically reduce calculation times, replacing tens of thousands of explicit solvent molecules (in biological fluids, water and dissolved ions) with much simpler models often based on continuum electrostatic theory, e.g. the Poisson or Poisson—Boltzmann partial differential equations (PDEs). Significant progress has been made to adapt PDE solvers to the incredibly demanding setting of molecular dynamics, but fast approximate models such as Generalized Born remain popular in many applications, due to their high accuracy and speed. Unfortunately, most of these fast models approximate Poisson and Poisson—Boltzmann models (which have well-known weaknesses) in a way that does not allow extensions to more advanced implicit-solvent theories, for instance involving nonlocal or nonlinear dielectric response. Therefore, to improve the accuracy and scalability of our simulations simultaneously, we must: (1) identify mathematical classes of models that can be computed using scalable algorithmic primitives, such as the fast multipole method; (2) develop approximation theories based on the underlying mathematical formalisms, e.g. variational interpretation of the Poisson equation; (3) extend these approximation theories to address more sophisticated physics, e.g. nonlocal dielectric theory or the fully nonlinear Poisson-Boltzmann equation. We have developed an approach called BIBEE (boundary-integral based electrostatics estimation) that meets all these challenges, providing a fast, mathematically rigorous, scalable, and future-proof electrostatic model for molecular physics