HYBRID QUANTUM AND CLASSICAL MECHANICAL METHODS FOR STUDYING BIOPOLYMERS IN SOLUTION

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1 Description of the Subject

Computer simulations can provide valuable insights into the structure, dynamics, and function of proteins and chemical reactions in solution. Undoubtedly, the key to success underlying these studies is to accurately describe their intramolecular and intermolecular interactions in solution. Empirical molecular mechanics potential functions have traditionally been used for the simulation of such large systems and much effort has been devoted to the parameterization of empirical potentials by studying small, model compounds that mimic the chemical groups in proteins and nucleic acids.

However, there are several well-known deficiencies in the molecular mechanics force fields in use today. First, empirical potential functions are not appropriate for studying chemical processes involving bond formation and breaking, which consist of electronic structural reorganizations. Secondly, electronic polarization effects are typically not treated explicitly in empirical potentials, which severely limit their reliability for describing processes such as substrate-enzyme binding and molecular recognition in aqueous solution. Although polarization terms may be included in the force field, there is no direct experimental data applicable for such a parameterization. Finally, empirical potential functions are not uniquely defined and are difficult to generalize for the application to new systems.

To overcome these difficulties, combined quantum mechanical and molecular mechanical (QM/MM) approaches have been proposed. In these methods, part of the system (for example, a solute molecule in solution or the active site region of an enzyme), is treated quantum mechanically. At the same time, the energy and forces for the remainder of the system (for example, the solvent molecules or rest of the enzyme) are calculated using a molecular mechanics force field. The use of a quantum mechanical method for the central part of the system means that the parameterization of a force field for that part is no longer necessary and, furthermore, means that electronic properties including bond formation/breaking and polarization effects are naturally determined by the molecular wave function. It is likely that advances in the methodology of hybrid QM/MM potentials shall greatly increase our ability to understand and to accurately predict intermolecular interactions in systems of biological interest.

2 The Aim of the Session

The use of the hybrid QM/MM potential in condensed phase simulations has only become possible very recently, thanks to advances in computer technology, statistical simulation methods, and quantum mechanical computational techniques. The hybrid QM/MM method has great potential in molecular modeling and in simulation to provide a consistent and an accurate description of intermolecular interactions in solution. To date, effort towards development of hybrid QM/MM methods has been largely centered on individual investigators and there has been a lack of meetings at which they can discuss problems specific to the area.

The aim of the minitrack on hybrid quantum and classical mechanical methods at the PSB is to assess the state-of-the-art in the field and to highlight areas for future research by bringing together researchers who develop hybrid simulation algorithms and apply them to biological systems.

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