Applications of the SemiEmpirical Born-Oppenheimer Molecular Dynamics (SEBOMD) approach to the study of biomolecules in aqueous solution: from small molecules to peptides and proteins

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Modeling large and reactive systems is still a challenging problem in modern computational chemistry. While full ab initio or Car-Parrinello molecular dynamics are demanding very high computational costs and are mostly limited to both "small" systems (i.e., around a couple of hundreds of atoms) and relatively short timescales (i.e., a few tens of picoseconds) even using supercomputers, QM/MM methods have proven nowadays to be among the most popular methods to tackle such problems. However, while very attractive in terms of computational costs, these multi-scaled methods suffer from some conceptual drawbacks mainly due to uncertainties on the way the QM and MM parts should interact: how electrostatics should be handled? How van der Waals interactions should be modeled? How frontier covalent bonds should be described? etc.

In the last version of Amber (Amber14) we have released what could be a third way to handle macromolecular systems for which the modeling of electronic and dynamical properties is required: the SEBOMD approach, standing for SemiEmpirical Born-Oppenheimer Molecular Dynamics. In this method, a whole system (e.g., a solute and its solvent in gas phase or encaged in a periodic box) is modeled at the full semiempirical NDDO quantum chemical level. Such a fast, albeit approximate, quantum method allows for the molecular dynamics simulations of rather large systems (today up to a thousand of atoms) for long simulations (in the nanosecond timescale) using commodity computers.

Here, we will present examples of applications of the SEBOMD approach to the modeling of the structure and the dynamics of biomolecules in aqueous solution: from small molecules (e.g., methane, ethanol, N-methylacetamide, ...) to a peptide (alanine dipeptide) and a protein (TrpCage). We will show that, provided one makes use of appropriate semiempirical parameters, the SEBOMD approach is capable of modeling correctly the electronic and dynamical properties of such systems.