

## QM/MM Solvation Using the Poisson-Boltzmann Equation

Seth A. Hayik, Ning Liao and Kenneth M. Merz Jr.

A method of solving the mixed quantum mechanical/molecular mechanical (QM/MM) Hamiltonian in solution, using the Poisson-Boltzmann (PB) equation to calculate partial charges and solvation free energies is presented. This method combines a linear scaling divide and conquer semi-empirical algorithm with the PB equation in a QM/MM framework, allowing only a specified region's charges to be polarized by the solvent while using fixed charges from a MM force field for the remaining system. This can save time over a full QM implementation, only requiring self-consistency to be achieved in a small QM region, while giving comparable results. The solvation free energy of several pentapeptides capped with an acetyl group (ACE) at the N-terminus and an N-methylamine group at the C-terminus (NME) were used to study the accuracy of this method as well as three small protein systems. The solvation free energies for the QM/MM implementation compare well with a full QM treatment of the same system, giving reasonable representations of the solvation free energy of the entire system. In the case of the pentapeptides the average error was only 4.9 kcal/mol with the smallest QM region. This mixed method will allow an accurate description of solvation effects in an area of interest, such as an active site, using mixed QM/MM Hamiltonians. Possible applications for this method include protein-ligand bind and reaction mechanism studies.