GPU accelerated QM/MM molecular dynamics simulations of biomolecular systems

Andreas W. Götz

San Diego Supercomputer Center, University of California San Diego, La Jolla, California, USA.

Mixed quantum mechanics / molecular mechanics (QM/MM) simulations couple the strength of quantum chemistry with the speed of molecular mechanics and thus enable simulations of local molecular properties and reaction mechanisms in complex environments such as enzymes and other condensed phase systems. However, QM/MM simulations are still orders of magnitude more computationally intensive than MM simulations, in particular if ab initio or density functional theory (DFT) Hamiltonians are employed. Efficient software implementations for modern computer architectures are thus essential to enable meaningful QM/MM molecular dynamics simulations. In this talk I will give an overview of QM/MM methods in the Amber software package for biomolecular simulations. I will focus on recent developments of QUICK and its integration with the molecular dynamics (MD) program sander, both of which are free and open-source programs distributed with AmberTools. QUICK is a quantum chemistry program for Hartree-Fock and DFT calculations with Gaussian basis functions that features an efficient implementation for massively parallel graphics processing unit (GPU) hardware. In QUICK the entire Fock matrix build and nuclear gradient calculation can be executed on single or multiple GPUs. This includes one-electron integrals (OEIs), two-electron repulsion integrals (ERIs), DFT exchange-correlation (XC) quadrature, and linear algebra operations. Both Nvidia and AMD hardware is supported. Efficient geometry optimizations are enabled via a recent integration of the open-source DL-FIND library, which includes both quasi-Newton based and more recently also machine learning-based optimizers. The interface of QUICK with sander enables high-performance ab initio QM/MM MD simulations including a range of free energy methods for the computation of reaction paths or binding free energies via alchemical transformations and bookending (end-point correction) methods. Importantly, the implementation in AmberTools 23 includes the ambient-potential composite Ewald method that incorporates long-range electrostatic interactions without truncation for condensed phase simulations under periodic boundary conditions. This integration makes it particularly easy to perform accurate QM/MM MD simulations without introducing numerical noise or neglecting potentially relevant electrostatic interactions between the QM and MM regions.