

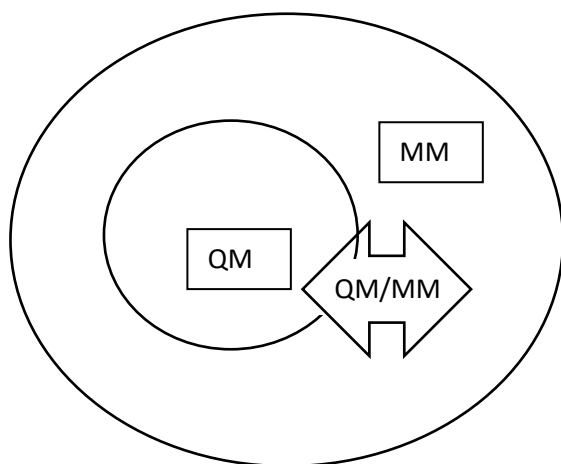
# Computational Chemistry I

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Text book Cramer: Essentials of Quantum Chemistry, Wiley (2 ed.)

## Chapter 7. Hybrid Quantum/Classical models (Cramer: chapter 13)

Last let us look in general terms how to combine the quantum and empirical modelling. Due to the Born-Oppenheimer approximation in QM system the atoms are treated classically when the electron wave functions are computed. This makes the QM/MM calculations "easy", one can treat all the atoms are classical ones.



We have good understanding of the QM part. The MM part will be discussed in details at the second part of the course. Here we need to know that the MM atoms have effective (non-polarizable) charge,  $q_i$ , Lennart-Jones (L-J) potential and some internal potential which include bond, angle and torsional potentials. The L-J potential is simple (it is atom centered and it has two parameter,  $\epsilon$  and  $\sigma$ )

$$V_{LJ}(r) = 4\epsilon \left[ \left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^6 \right]$$

Different  $\epsilon$  and  $\sigma$  are given for each atom type  $\epsilon_i$  and  $\sigma_i$  (Note there can be several different C, O etc. atoms.). For mixed atom type interactions mixing rules are used:

$$\epsilon_{ij} = \sqrt{\epsilon_i \epsilon_j} \quad \sigma_{ij} = \frac{1}{2}(\sigma_i + \sigma_j)$$

When we know the MM atom positions we know the electrostatic potentials they will case (in the QM region)

$$V_{el,MM \rightarrow QM}(r) = \sum_I \frac{q_I}{|r - R_{MM,I}|}$$

Then the total atomic potential is

$$V_{el}(r) = - \sum_I \frac{Z_I}{|r - R_{QM,I}|} + \sum_I \frac{q_I}{|r - R_{MM,I}|}$$

Now one can solve QM electronic problem with this potential. The situation with the L-J interactions is a bit more difficult. It is not easy to get the L-J parameters from the QM calculations. Sometimes the L-J MM field is ignored in the QM region or the MM parameter are used to model the MM L-J effect to QM atoms. Note inside the QM the L-J parameters are not used.

### QM/MM interphase

In the QM/MM modelling the QM/MM interphase require own model. The MM part will see the QM electrostatic potential but it will be very time consuming to compute the  $V_{el}(r)$  at every MM atom position. One solution is to use QM derived charges for the atoms. Then

$$V_{el,QM \rightarrow MM}(R_{MM,J}) = \sum_I \frac{q_I^{QM}}{|R_{MM,J} - R_{QM,I}|}$$

The L-J is usually done with MM parameters for the whole system so MM system sees the QM atoms with empirical L-J parameters.

If the QM molecule do not form covalent bond with the MM region the situation is rather easy. The models above works quite well, but if there is a bond between the regions it should be a single bond. The dangling single bond in the QM part can be terminated

with a hydrogen, methyl or a simple model potential. (The terminating group is not included to rest of the models. Confusing isn't.) One also need to extend the MM potentials, like torsional potentials, to the QM region.

Another complication is the polarization. In QM region it is naturally taken into account but in the MM region the models are usually non-polarizable. This is not consistent and it would be good to have polarizable model also in the MM part. Unfortunately, the polarizable MM models are rare.

As one can see from the Orca manual, the QM/MM modelling is not easy. One need to have understanding from both modelling fields. On the other hand, now many of the most used modelling programs, like Orca and GROMACS support QM/MM models. Thus is it become easier to do them and the QM/MM approach provides a new and more realistic way to model the solvation. Obviously, the QM/MM is much more general than the continuum solvation models. It takes into account the molecular structure of the "solvent". It can handle hydrogen bonds, non-homogenous solvent, dynamics of the solvent, etc.

## Ab initio molecular dynamics

One can also include molecular dynamics (AIMD) to quantum chemistry. It is very easy since we can compute the forces and the BO approximation allow classical treatment of the atoms. Now the dynamics can be described with Newton's equation

$$F = ma$$

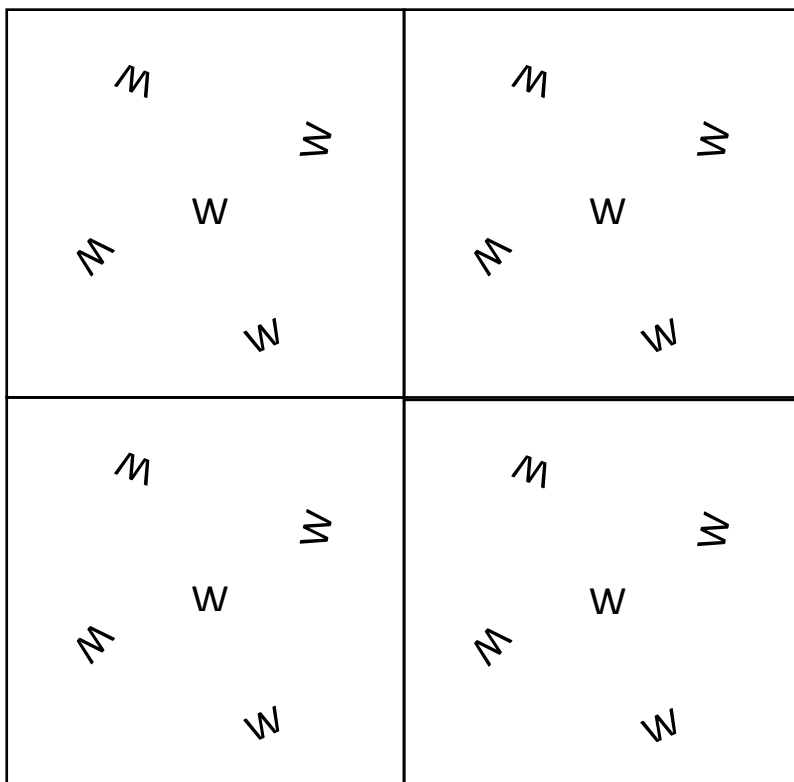
With given atom configuration we can compute the forces and update the atomic positions with some algorithm. One of the simplest ones is the Verlet algorithm

$$R_I(t + \Delta t) = 2R_I(t) - R_I(t - \Delta t) + \frac{F_I(t)}{m_I} \Delta t^2 + O(\Delta t^4)$$

The main point is that the position update have to be done very often. The  $\Delta t$  is very small, typically 1 fs. So to simulate 1 s we need  $10^{15}$  steps! That is not possible but of course, shorter

simulation times are possible. In AIMD the simulation time scales are ca. 100 ps (and up to 1 ns = 1 milj. steps). Note that CPU time for an AIMD step is around 10s. Naturally, the size of the system affect a lot of the total time scale. In AIMD systems of few 100 water molecules can be simulated. (And this is hard to improve due to the  $N^3$  scaling of the DFT methods.)

The MD is seldom relevant for a single molecule. The internal motion of a small and medium molecules are quite well described with vibrations. Cluster of molecules are more interesting but not very relevant in chemistry. The most important application is liquids and solution effects. The most convenient way to model the liquid is to use periodic boundary conditions (PBC).



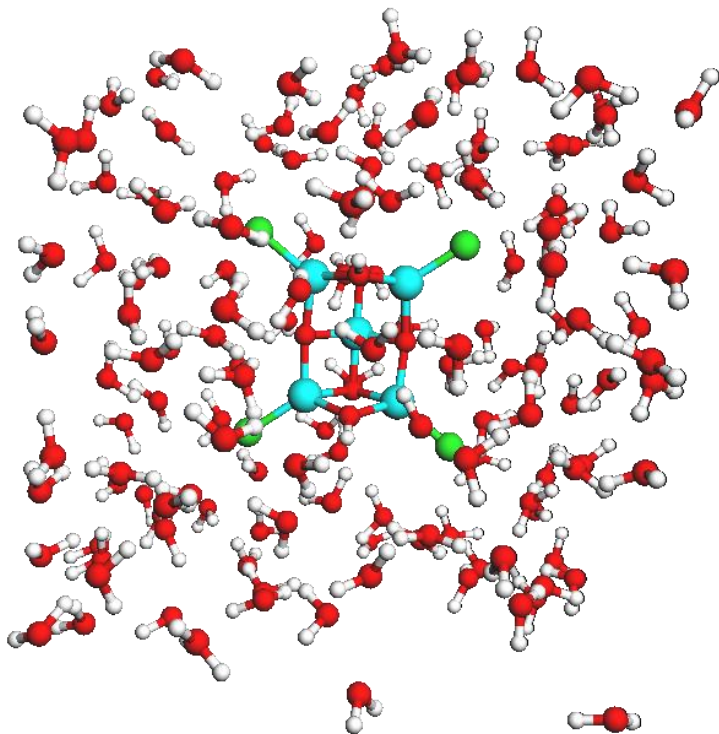
In periodic boundaries the system is repeated in every direction. One need to compute the forces with the PBC but it is enough to simulate only one "box". The PBC works only for neutral systems (details in the other part of the course). The DFT equations are easy solve with PBC but HF is more difficult. Only very recently periodic MP2 and CCSD has been implemented.

In general, all simulation techniques, like thermostats, barostats, thermodynamical integration etc, that have been developed for empirical MD can be used for AIMD.

## Applications

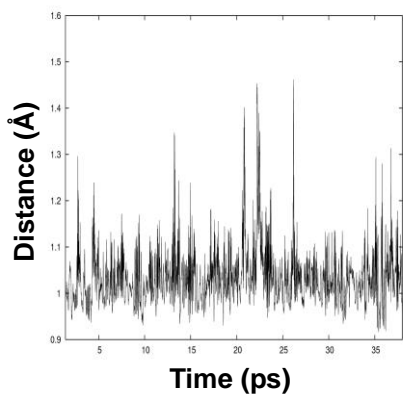
Water, water, and water. The most obvious AIMD application is water and molecules in water. Almost any small system (up to ca. 500 waters and solvent of tens of atom) can be simulated.

$\text{Al}_5\text{O}_x\text{Cl}_4$  AIMD simulations, periodic 17 Å cubic box, 141  $\text{D}_2\text{O}$  molecules. The PBE GGA + empirical van der Waals corrections were used.

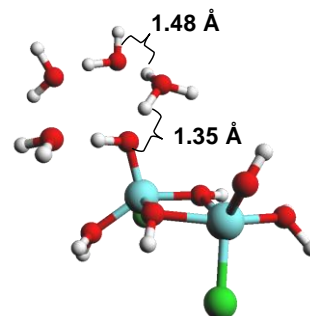
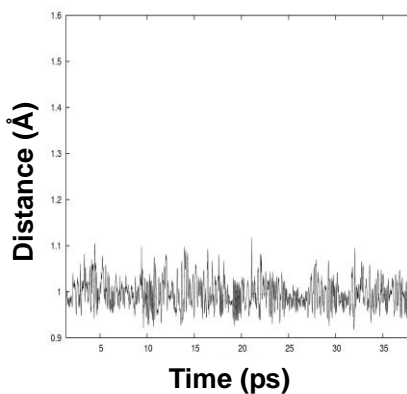


One particularly interesting application is acidity and protons. Below is an example of a water molecule bound to Al atom. The proton in the water is weakly bond and it can occasionally dissociate but it will always come back (within this simulation). The simulation time is 40 ps.

loosely bound proton (acidic)

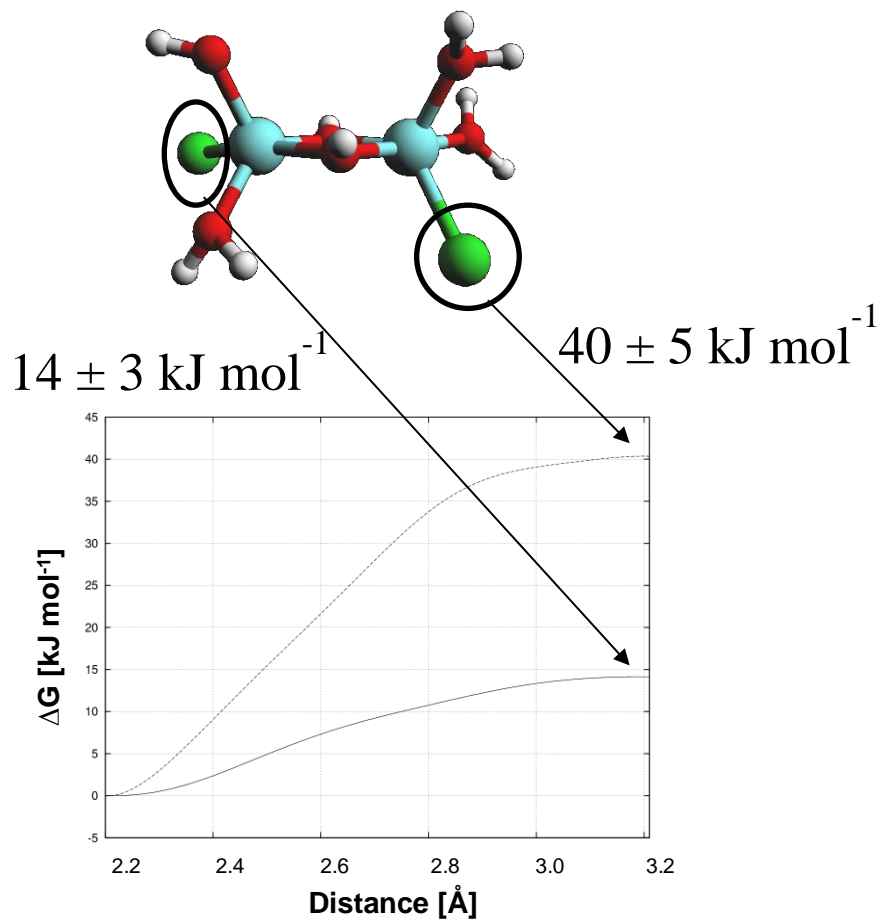


normal proton (water)



One can even estimate the pKa from the proton fluctuations.

In addition, reaction barriers can be estimated using the thermodynamic integration method. Here the constraint force algorithm has been used.



Also some other solvent than water, like methanol, ammonia, can be simulated but the computational cost increases rapidly and in addition the needed time scales are longer than in water.