Characterization of S_N2 in CP2K

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This study was aimed at characterizing the simple S_N2 reaction of CH_3Cl in vacuum, using quantum mechanics (QM) molecular dynamics (MD) simulations. This work was built on that done by K. Fleming[1] using AMBER software, aimed at replicating her results using CP2K software.

While these reactions typically occur on long time scales, the use of enhanced sampling methods can extend the typically accessible simulation time of MD simulations. An example of such is MetaDynamics (MetaD), which deposits a history dependent bias potential as a function of the chosen collective variables (CV). This bias allows for the exploration of high energy states in a controllable manner, within an accessible simulation time. In the long time limit, MetaD provides an estimate of the underlying free-energy surface (FES). Well-tempered MetaD is a flavor of MetaDynamics, which uses a progressively damped bias. In well-tempered MetaD the rate of bias deposition decreases as a function of time. The use of a this converging bias, implies convergence, reducing the need to manually observe differences between free energies of separate basins to check for overall convergence of the FES.

In the method coined by Fleming[1] as infrequent metadynamics, dynamic information can be extracted from biased simulations. Under the assumption that no bias is deposited in the Transition state region, and that the dynamics are Markovian in nature, the following acceleration factor can be calculated from:

$$\alpha(t) \approx \frac{Z_0}{Z_M} = \langle e^{\beta[V(s(\mathbf{R}),t)]} \rangle_M,$$

Where Z_0 is the partition function for the system confined to the first basin, and Z_M is the partition function in the first basin, sampled using the time dependent probability density of MetaD. Extracting this factor is now easily implemented in PLUMED software. Transition time over an energy barrier is then found by the following equation.

$$t^{\text{eff}} = \sum_{i=0}^{N} \Delta t_i^{\text{MetaD}} e^{\beta V_{\text{bias}}(s,t)}$$

The rate of a rare event (i.e reaction rate, ν) is simply the inverse of an ensemble average of transition times, and can be calculated post priori.

Methods

These simulations were set up using PM6 level of theory in the CP2K program. Simulations were performed with a 1fs time step until a rare event occurred. The two C-Cl bonds were biased, using restraints to keep the heavy atoms within 0.6 nm. Biased simulations were performed in PLUMMED, using the well-tempered variant. The bias factor was set to 9, Gaussian width of 0..0025 nm was used, the initial hill height was 0.3 kJ/mol, and a stride of 20 ps was used.

Results

The following table shows the effective times calculated from CP2K, compared against those done in AMBER. As shown, the results are in close agreement. Errors are probably due to the small sample sizes used.

Table 1: Results from CP2K and AMBER

	CP2K				AMBER (Fleming[1])			
Temp	**t_eff (ns)**	**error**	**p-value**	**events**	**t_eff (ns)**	**error**	**p-value**	**events**
1200	0.025	7.97E-03	0.394	122	0.0427	1.90E-03	0.386	1170
1000	0.041	9.59E-03	0.949	114	-	-	-	-
900	0.071	2.34E-02	0.970	187	0.116	7.30E-03	0.473	432
750	0.140	2.26E-02	0.775	121	-	-	-	-
600	0.294	5.80E-02	0.883	128	0.457	2.70E-02	0.909	631
600*	0.463	8.61E-02	0.910	62	-	-	-	-

* indicates Metadyamics run

The following graph shows the reaction rates obtained in CP2K, vs in Amber. In CP2K activation energy was determined to be around 6.4kcal/mol, using all data points. Fleming cites values from ~6.7 to 7.0 kcal/mol.

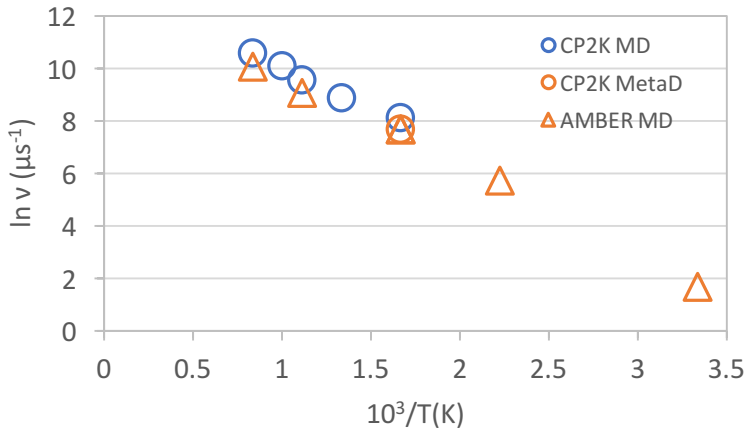

Figure 1: Arrhenius plot of the inverse temperature (K) versus the log of the reaction rate, ν

Conclusions

The results of the Fleming paper were replicated with accurate results to some degree showing CP2K to be a powerful program to run these simulations at even higher levels of theory. Concerns with CP2K would be its high memory usage and long simulation time, effects which could amplify with use of higher levels of theory. This was apparent in the low temperature simulations, which crashed frequently due to the long simulation times involving high memory usage. Further investigations into CP2K's memory performance would be needed to make accurate recommendations.

References

[1] Fleming, K. L., Tiwary, P. & Pfaendtner, J. A New Approach for Investigating Reaction Dynamics and Rates with Ab Initio Calculations. *J. Phys. Chem. A* **120,** 299–305 (2016).