Towards the understanding of the structure and formation of Deep Eutectic Solvents using classical molecular dynamics and fragmentation simulations

Forcefield parametrization and benchmarking the density functional approximation methods.

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1 Introduction

The invention of DES lead to the studies of wide-range of applications as their nature and tailoring help in significant processes. The modeling of DES as helps as they explain the experimental observations and help in the design of DES. In this thesis, the DES systems considered are:

1. Urea - Choline Chloride (1:2 molar ratio) colloquially called Reline.
2. Evernic Acid - Usinic Acid NADES found in the lichen *EverniaPrunastri*

And the following modeling strategies/tools were utilised for this purpose:

1. Molecular Dynamics
2. Fragmentation Simulations

2 Summary of third year work

Since the last CSI, the following projects were undertaken and certain protocols and work flows were developed based on the benchmarking of certain semi-empirical and density functional approximation methods. The following projects were undertaken:

1. **Developing the algorithm for fragmentation simulations of non-covalent clusters**
2. Studying the stability and water retention properties of the proposed NADES systems in lichen EverniaPrunastri.

3 Metadynamics xTB/CREST workflow benchmarking

3.1 Benchamarking at Semiemperical level with CREST

Three different initial coordinates were choosen for the cluster combination $[3Ch+3U+4Cl]^{-1}$. workflow: The initial coordinates were used as input for the NCI algorithm of CREST, that performs iMTD sampling. The energy of the conformers was calculated at GFN2-GFNFF composite method level to preserve the topology of the system. The conformers that fall in the energy range of 12 kcal/mol from the lowest energy conformer were selected and further optimized at GFN2 level of theory.

3.2 Benchamarking at DFT level with CENSO

The ensemble of conformers generated from the previous step were used as input for two types of calculations in CENSO:

1. Single point energy calculations of each conformer at B97-3c level of theory (called *part0* calculations in CENSO).
2. Geometry Optimization of all conformers at r2scan-3c level of theory (called *part2* calculations in CENSO).

It was verified that the threshold energy value (the free energy value above which the conformer is ignored by CENSO) for optimization calculations was set very high so as to not ignore any conformers in the optimization calculations.

4 Benchmarking density functional approximations

List of available methods and codes for speeding up the optimization calculations:

1. ORCA (DFA and composite methods)
2. CENSO (with ORCA as the QM calculation driver and xTB as the semi-empirical method; parameters already benchmarked by Grimme's lab)
3. ML-based methods (AIQM1 method in MLatom 3)

5 Local Energy Decomposition

5.1

Systems Studied:

1. $[1Ch + 1U + 2Cl]^{-1}$ $(m/z = 235)$
2. $[1Ch + 2U + 2Cl]^{-1}$ $(m/z = 295)$
3. $[1Ch + 3U + 2Cl]^{-1}$ $(m/z = 355)$
4. $[2Ch + 0U + 3Cl]^{-1}$ $(m/z = 313)$

Initial coordinates	**Energy (Hartree)**	**Time (s)**	**Number of conformers generated**
1			
2			
3			

Table 1: Energy of the most stable conformer after optimization at GFN2 level of theory

Initial ensemble	**Energy (Hartree)**

Table 2: Single point energy of the most stable conformer from *part0* calculations of CENSO

Initial ensemble	**Energy (Hartree)**

Table 3: Energy of the most stable conformer from *part2* calculations of CENSO

Method	Implementation	directory of input file

Table 4: Various approaches for optimization with ORCA/CENSO and the corresponding computation times on the 32-core Intel Cascadelake machine.