Point-by-point Revisions

Reviewer 1 Comments:   
  
This manuscript evaluates the performance of the effective fragment potential for the intermolecular interactions in ionic liquids by comparing the results term by term to results from symmetry adapted perturbation theory (SAPT). The authors employ two model IL families based on imidazolium and pyrrolidinium based cations with eight different anions. Overall, this is a paper that presents interesting insights and should be suitable for publication after the issues below have been addressed:   
  
The most important issue to be addressed is the term-by-term comparison. As stated by the authors in pp. 10 "Polarization in EFP is analogous to induction in SAPT with one exception. The SAPT induction term also contains the charge-transfer energy ..."   
Thus, SAPT does not separate the charge transfer, e.g. JCP, 140, 094106, 2014. Therefore, the one-to-one comparison for each of the second order terms is slightly misleading. Especially since there is not one single way to decompose the energy and EFP is based on a variational decomposition (not perturbational). Therefore, it is recommended that the authors also compare the sum of the polarization and charge transfer from EFP to induction from SAPT, as well as provide a more thorough explanation of the errors in the total intermolecular interaction energy 

* *fundamental difference in definition of charge-transfer*
* *charge-transfer in SAPT is meant to vanish in the complete basis set*
* *Adding charge-transfer with EFP polarization has very little effect on the analysis.*
* *How CT behaves wrt basis set in EFP (min and max CT, CT/Ind% (EFP each basis set)*
* *Analysis for the 2nd order terms was not done for induction and polarisation for the above reasons, as this difference between was not observed.*
* *Flick et al. (JCTC, 8, 2835, 2012) did not compare SAPT induction with EFP polarisation + CT, saying it is insignificant for dispersion-dominated complexes, but may be significant*

*This is an important point raised, and one that we admit was not adequately treated in the manuscript. It comes down to the fundamental difference of definitions of the charge-transfer energy.*

*The theoretical background section has been amended to emphasise this.(not yet tbh)*

*Due to this discrepancy, the rational route to take would be to compare EFP(Polarisation + Charge-Transfer) with SAPT(Induction), and this was what we initially tried. However, this was found to have very little difference with the EFP(Polarisation)—SAPT(Induction) comparison. Furthermore, in the SAPT definition, charge-transfer*

-The authors neglect to cite several potentials for ionic liquids that are based on energy decomposition analysis such as those developed by the group of J.R. Schmidt (JPCL, 5, 2670, 2014) or the AMOEBA potential for ILs (JPCB, 118, 7156, 2014) or other polarizable IL potentials such as APPLE&P from the Borodin group. 

*Section1, pp. 2: Mention of work done with force fields on ionic liquids has now been included in the introduction.*

-subsection 2.2, pp. 10: There is no mention of the overlap damping employed in EFP to account for penetration effects in the Coulomb and Polarization terms. 

*Subsection 2.2, pp. 11: Overlap damping is now mentioned for the Coulomb, Polarisation, and Dispersion terms.*

-pp. 14, subsection 3.0.3: The authors could cite the work by Sherrill et al (JCP, 140, 094106, 2014) to justify the SAPT level employed for the reference.

*Subsection 3.0.3, pp. 15: Mentioned the work done by Parker et al. in Sherrill’s group used their findings to justify our choice of basis set for SAPT2+3.*  
  
-pp. 16 top, it is unclear what is being compared for the differences between the basis sets. What do the authors mean by Coulomb being underestimated by 2.7 kJ/mol in triple zeta? what is the reference?

*Subsection 3.0.3, pp. 17: Sentences have been rewritten for greater clarity.*  
  
-Table 3: define acronyms 

*Table 3: Acronyms for typical ionic liquid anions (TILAs) and halides (Hal) had previously been mentioned in subsection 3.0.1 on pp. 12, but have not been used in any tables up to section 4.1 on pp. 17 in Table 3. For the readers’ convenience, the revision includes a reiteration in the table’s captions as to a reminder.*

-Table 4: define units (e.g. in caption)

*Table 4: Added units to captions.*   
  
-Figure 4: It is unclear which data corresponds to the raw results, and which to the scaled. This figure needs to be re-worked.

*Figure 4, pp. 26: Figure has been reworked, with all the distributions as density distributions (replaced histograms). Raw differences between SAPT and EFP are solid line unfilled densities, whereas the filled distribution represent differences after scaling.*

Reviewer 2 Comments:   
  
The authors present a very thorough comparison of the effective fragment potential method (EFP) for its use to describe the interaction in isolated ionic liquid ion pairs in the gas phase. As benchmark, SAPT2 and SAPT2+3 were used, which can be regarded as state-of-the-art. It was found that the performance of EFP depends much on the choice of the basis set and it is hard to predict only from the zeta-level and choice of augmented and polarization functions whether a certain basis set will work well. Overall, the performance of EFPs for ionic liquid ion pairs was worse than anticipated. A detailed analysis of the individual interaction components will enable the future development of improved EFP potentials for ionic liquids. The paper is well-organized and will enable the further improvement of methodology for the efficient simulation of ionic liquids, which is a very important subject and therefore the MS can be recommended for publication in JCTC after the following minor corrections are performed.   
  
1. Please upload the ESI. It was missing in this submission. 

*The ESI (esi.pdf) was in the “tex” folder. It has been moved next to the manuscript now. To generate the pdf from the .tex file, use “esi.tex” in the “tex” folder.*

2. Figures 1 and 2: It is hard to see the geometry. Perhaps two views (top and side, or similar) would be more helpful. In Figure 1: Is p1 a stereoisomer of p4? Also, it does not make sense to indicate double bonds in the imidazolium ring. Perhaps a schematic figure might serve better overall.

*Figs. 1 & 2: Reworked, hopefully the orientation and nature of the interactions are clearer to reader.*  
  
3. Only optimized geometries were used, but it is questionable whether optimized geometrical parameters for ion pairs are useful as they come in all ranges in the real liquid. This reviewer wonders if non-optimized geometries would show different trends in the performance than optimized geometries. 

*~~This is an interesting point. Indeed, in the real physical world, the ions comprising an ionic liquid would exist in a state of constant flux between different interacting geometries. In an ideal world, we would like to calculate interaction energies at every point on the potential energy surface. However, due to the limitations of our current technology, the computational expense associated with such an exercise would be astronomical. In light of this, calculations are performed only at selected points on the potential energy surface. Furthermore, only a single ion pair in gas phase is examined, as larger systems are currently intractable. These select points on which calculations are to be performed are located through geometry optimization, the idea being that, the system, which obeys the Boltzmann distribution, would spend a greater portion of the time in energetically favourable geometries.~~*

*~~This work focuses on the behaviour of the EFP method relative to SAPT. To answer the reviewer’s question, we would hope that this analysis is geometry independent. That is, regardless of the geometry being considered, the same trends would be observed between the potential energy surfaces of EFP and SAPT. However, it is highly possible that, in non-optimised geometries, an interaction that is usually non-dominant becomes dominant, and as such the differences in how EFP and SAPT treat such instances may not be inferable from the differences between EFP and SAPT for optimised geometries. “Usually” being determined in the context of a Boltzmann distribution.~~*

*To answer this point, we have calculated EFP and SAPT energies for c1mim-bf4 and c1mpyr-bf4 at 2 unoptimised separations, +0.6 and +1.0 Angstroms. The raw energies are reported below in Tables 1 & 2. Only the SAPT2+ level is used due to limitations in time. The differences and percentage differences are also presented, in Tables 3 & 4. The difference is defined as E(Diff) = E(SAPT) – E(EFP), whereas the percentage difference is E(%Diff) = E(Diff)/E(SAPT)\*100. Note that the percentage differences are reported unsigned, i.e. all positive.*

*Considering the raw energies, we see that as the separation between the ions increase, the strength of each interaction decreases too, as expected. This is observed for both EFP and SAPT, and is reflected in the difference of raw energies and the percentage differences as well. The percentage and raw differences appear to vanish as the interionic distance increases. For electrostatics, while the absolute differences are larger than for the other contributions, the relative differences are smaller. On the other hand, for exchange, and to a smaller extent for induction and dispersion, while the absolute differences decrease dramatically with respect to increasing distance, the percentage difference does not drop quite as rapidly. For example, for [C1mpyr][BF4], going from +0.6 to +1.0 Angstroms, the difference between SAPT and EFP for exchange goes from 7.6 to 1.7 kJ/mol. However, the percentage difference only reduces from 31.1% to 26.2%. These percentage differences are quite high. The reason why they remain so high is because of the smaller exchange energies, which are more sensitive to small differences.*

*From this, we deduce that, in terms of absolute difference, SAPT and EFP would have better agreement at longer separations on the PES mostly because interactions weaken and the magnitudes decrease. However, the relative differences between the two methods do decrease as well, albeit slower and with less regularity.*

Table . EFP energies (kJ/mol)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| EFP | Elst | Repl | Pol | Disp | CT | Total |
| [C1mim][BF4] (Re+0.0) | -392.9 | 71.5 | -32.7 | -55.6 | -2.5 | -412.1 |
| [C1mim][BF4] (Re+0.6) | -345.1 | 20.6 | -23.9 | -23.8 | -0.5 | -372.7 |
| [C1mim][BF4] (Re+1.0) | -314.0 | 6.1 | -17.8 | -13.5 | -0.1 | -339.3 |
| [C1mpyr][BF4] (Re+0.0) | -376.3 | 63.2 | -37.6 | -43.0 | -4.3 | -398.0 |
| [C1mpyr][BF4] (Re+0.6) | -325.0 | 16.8 | -26.1 | -17.8 | -1.1 | -353.1 |
| [C1mpyr][BF4] (Re+1.0) | -294.0 | 4.9 | -18.6 | -9.8 | -0.3 | -317.8 |

Table . SAPT energies (kJ/mol)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| SAPT | Elst | Exch | Ind | Disp | CT | Total |
| [C1mim][BF4] (Re+0.0) | -431.2 | 163.0 | -50.0 | -59.0 | - | -377.1 |
| [C1mim][BF4] (Re+0.6) | -339.7 | 28.4 | -27.8 | -24.5 | - | -363.6 |
| [C1mim][BF4] (Re+1.0) | -309.6 | 8.5 | -19.7 | -13.7 | - | -334.5 |
| [C1mpyr][BF4] (Re+0.0) | -414.9 | 158.0 | -61.2 | -53.2 | - | -371.3 |
| [C1mpyr][BF4] (Re+0.6) | -323.4 | 24.4 | -29.9 | -20.3 | - | -349.2 |
| [C1mpyr][BF4] (Re +1.0) | -293.0 | 6.6 | -20.4 | -10.9 | - | -317.7 |

Table . Differences between SAPT and EFP energies: E(SAPT - EFP) (kJ/mol)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Differences (kJ/mol) | Elst | Exch | Ind | Disp | CT | | Total |
| [C1mim][BF4] (Re+0.0) | -38.3 | 91.5 | -17.3 | -3.4 | - | 35.0 | |
| [C1mim][BF4] (Re+0.6) | 5.4 | 7.8 | -3.9 | -0.7 | - | 9.1 | |
| [C1mim][BF4] (Re+1.0) | 4.4 | 2.4 | -1.9 | -0.2 | - | 4.8 | |
| [C1mpyr][BF4] (Re+0.0) | -38.6 | 94.8 | -23.6 | -10.1 | - | 26.7 | |
| [C1mpyr][BF4] (Re+0.6) | 1.6 | 7.6 | -3.8 | -2.6 | - | 4.0 | |
| [C1mpyr][BF4] (Re+1.0) | 1.0 | 1.7 | -1.8 | -1.1 | - | 0.2 | |

Table . Percentage differences: E(SAPT - EFP)/E(SAPT) (kJ/mol)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Relative Differences (%) | Elst | Exch | Ind | Disp | CT | Total |
| [C1mim][BF4] (Re+0.0) | 8.9 | 56.1 | 34.6 | 5.7 | - | 9.3 |
| [C1mim][BF4] (Re+0.6) | 1.6 | 27.6 | 13.9 | 2.7 | - | 2.5 |
| [C1mim][BF4] (Re+1.0) | 1.4 | 28.4 | 9.9 | 1.2 | - | 1.4 |
| [C1mpyr][BF4] (Re+0.0) | 9.3 | 60.0 | 38.6 | 19.1 | - | 7.2 |
| [C1mpyr][BF4] (Re+0.6) | 0.5 | 31.1 | 12.6 | 12.6 | - | 1.1 |
| [C1mpyr][BF4] (Re+1.0) | 0.3 | 26.2 | 8.8 | 10.2 | - | 0.0 |

4. It would be helpful to indicate the amount of charge transfer between the ion pairs, in terms of some population analysis such as Weinhold's NPA. The authors noted that this is of great concern for the development of classical and coarse-grained potentials.

*Our group has previously done NPA charge-transfer calculations on ionic liquids (Rigby & Izogorodina, PCCP* ***15*** *1632 2013). The results indicate that NPA gives very small NCT (Fig. 7, pp1640), except for the chloride anion. Due to the localised orbitals used in NPA, it treats covalent interactions well, but not so much for systems where Coulombic interactions dominate. The reason the chloride anion performs better is because of the small size of the monoatomic anion which leads to greater orbital overlap. This renders the interaction semi-covalent, and hence NPA produces non-negligible charge-tranfer comparable with other atomic partial charge schemes. With this in mind, we decided not to use NPA alongside with the geodesic scheme to quantify the NCT in the studied systems, since aside from bromide and chloride, the interaction character of the anions is mostly noncovalent.*