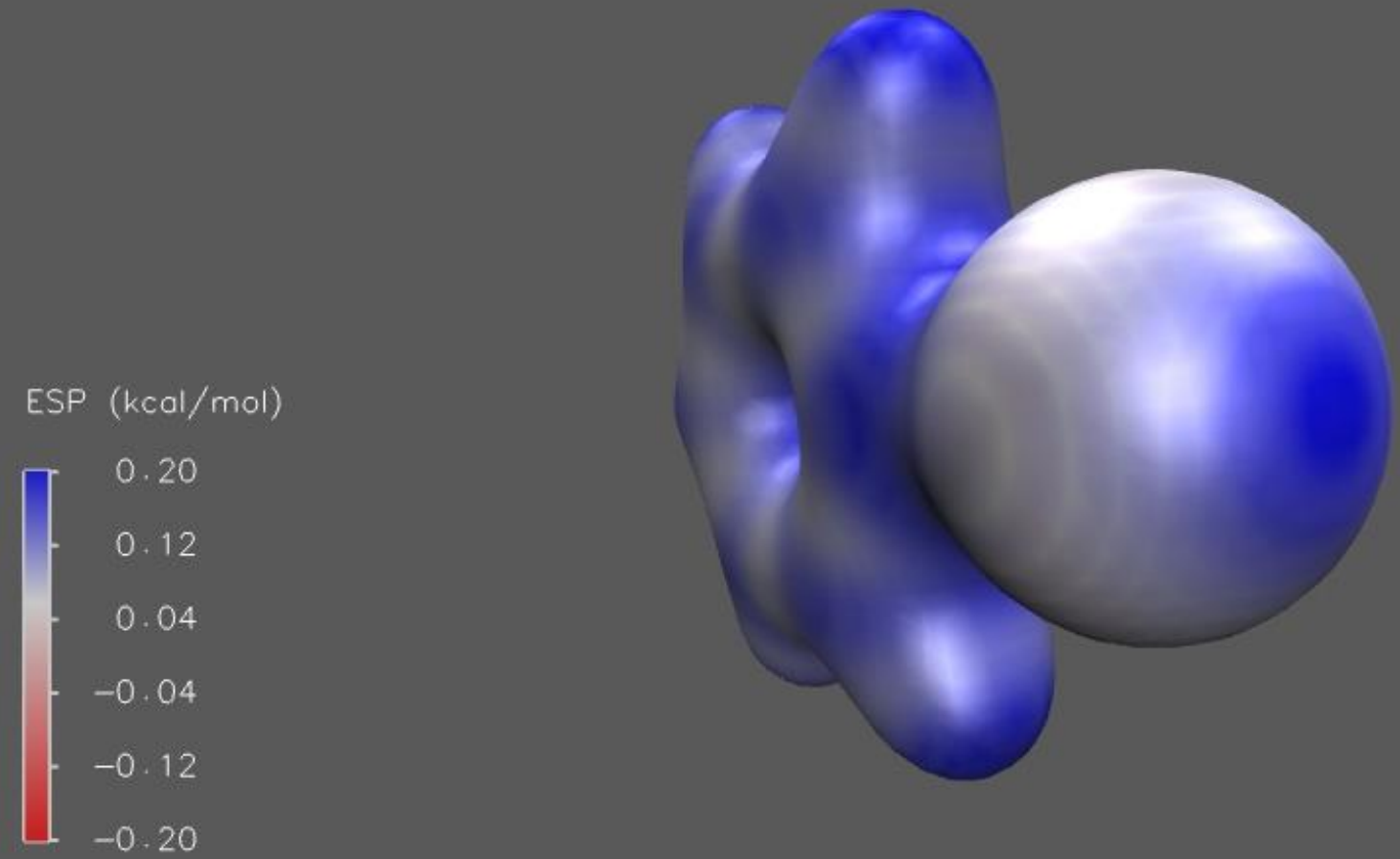
IGC Group Talk 2017-12-13 by Lukas Schreder, Research Project I

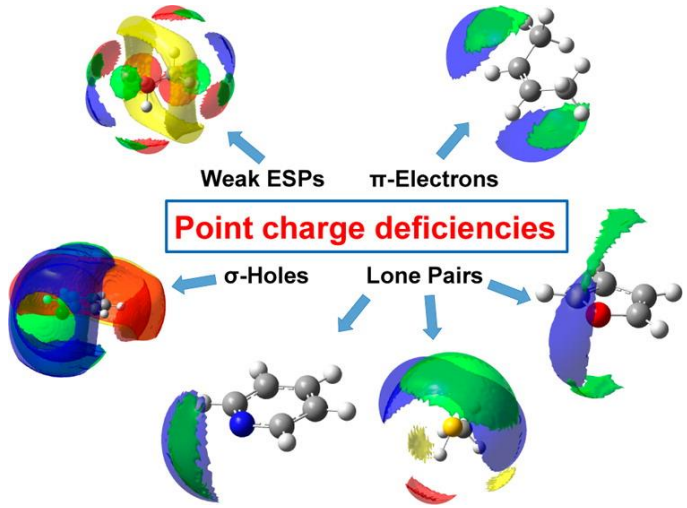
Deriving Off-site Charge Parameters to Model Anisotropic Charge Distributions in Phenyl Halides



PhCl
MP2/Def2TZVP

Point Charges Fail to Reproduce Critical Electronic Properties

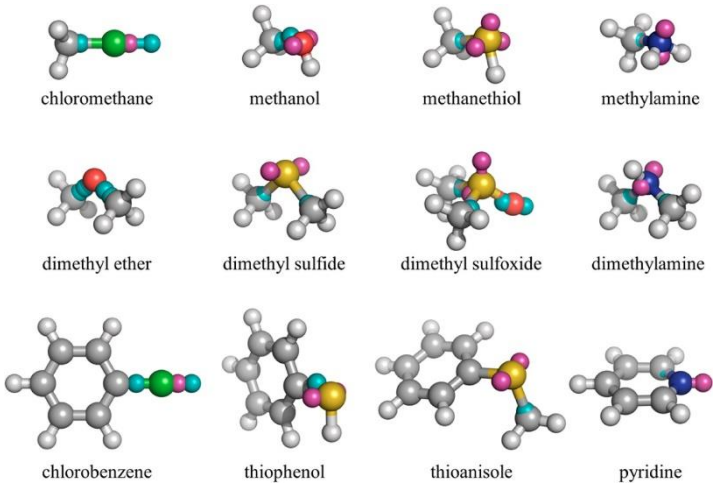
- Charge anisotropies are often neglected in MD
- Many forcefields support Virtual Sites (but not all, e.g. GAFF), which are often used as a makeshift solution
- Almost all heteroatoms require multipole descriptions



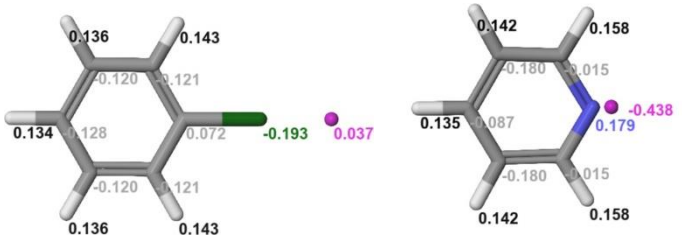
Kramer et al.; *J. Chem. Theory Comput.*, 2014, 10 (10), pp 4488–4496

Previous Approaches are Expensive to Compute

- Cole et al.: Simplex minimization against RMSE of Dipole and Quadrupole moments with up to 3 virtual sites per atom
- Harder et al.: Fitting against ESP error and MD data (hydration free energy)



Cole et al.; *J. Chem. Theory Comput.*, 2016, 12 (5), pp 2312–2323



Harder et al.; *J. Chem. Theory Comput.*, 2016, 12 (1), pp 281–296

Correcting Fundamental Electronic Properties with Off-site Charges

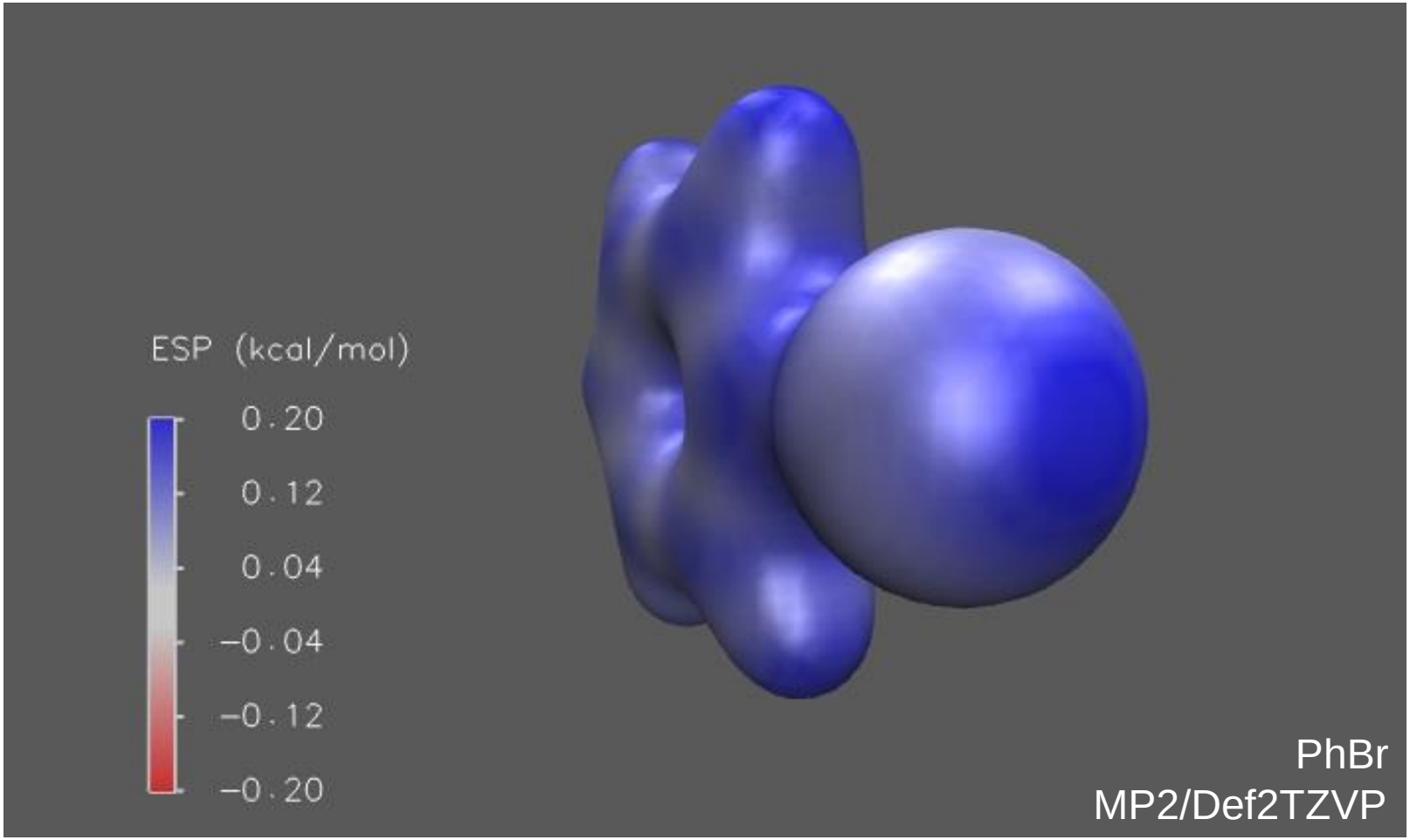
- DDEC-based charge partitioning introduces 10-20 % error in molecular dipole moment

$$\int_V \rho(r)(r - r_{COM})\ d^3r$$

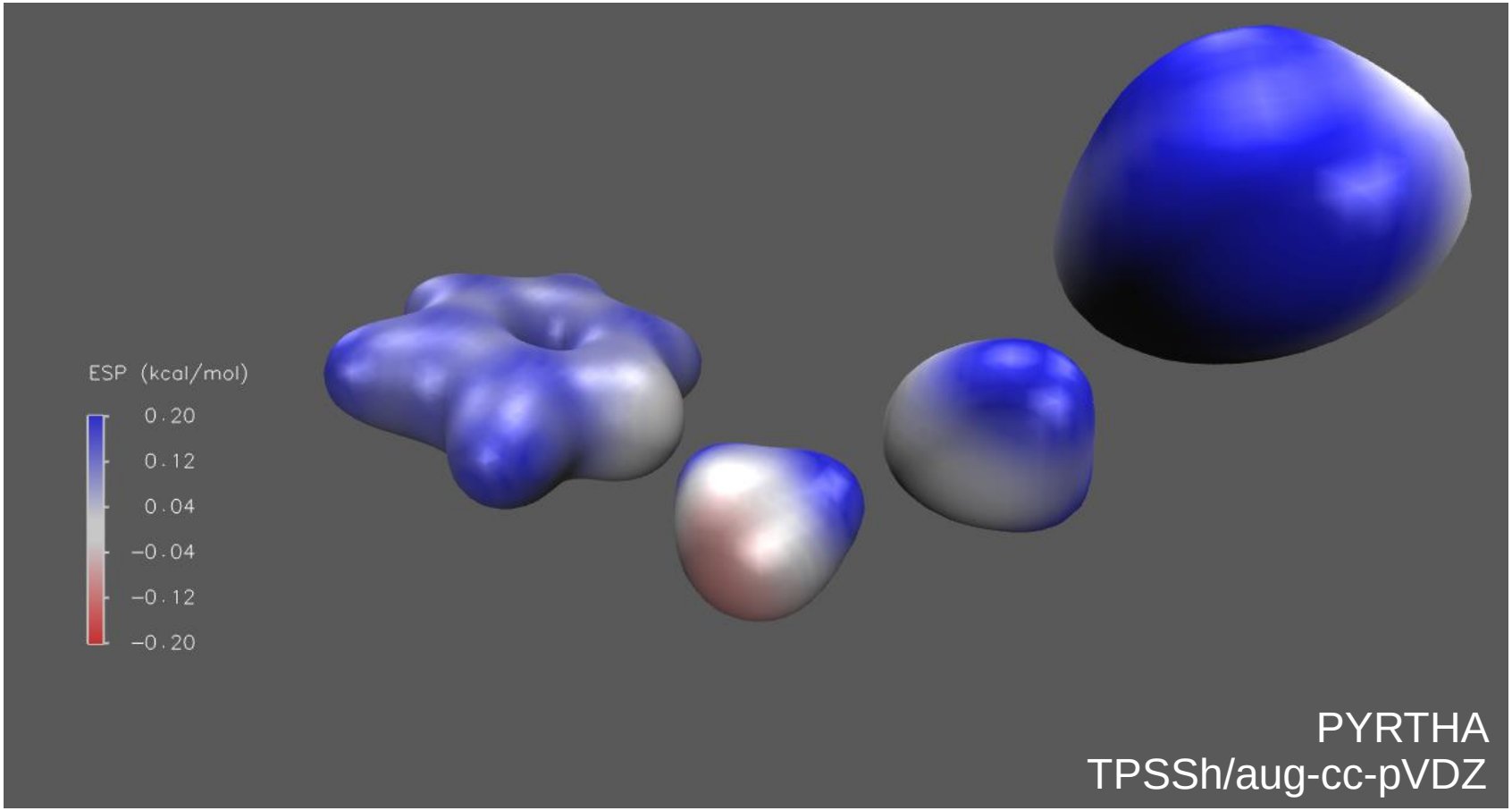
$$\sum_{i=1}^{N} q_i\ (r_i\ - r_{COM})$$

- What if we place off-site charges to minimize this error and minimize the result against ESP error?

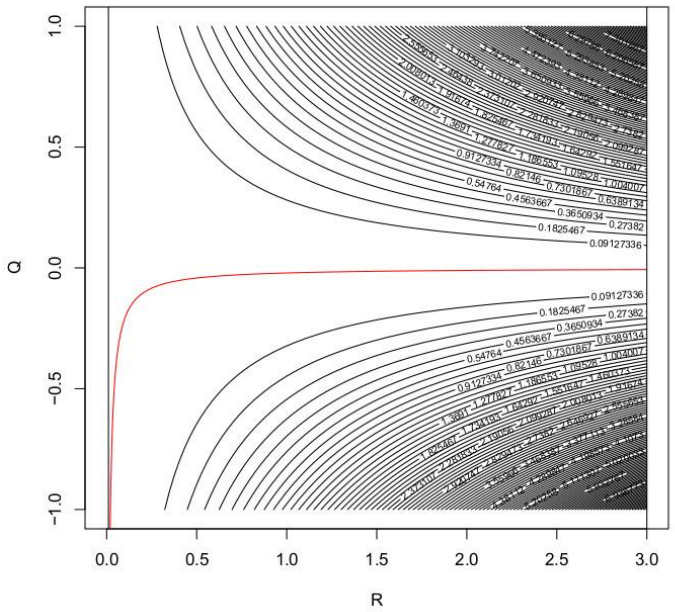
Finding Possible Use Cases: Halogens

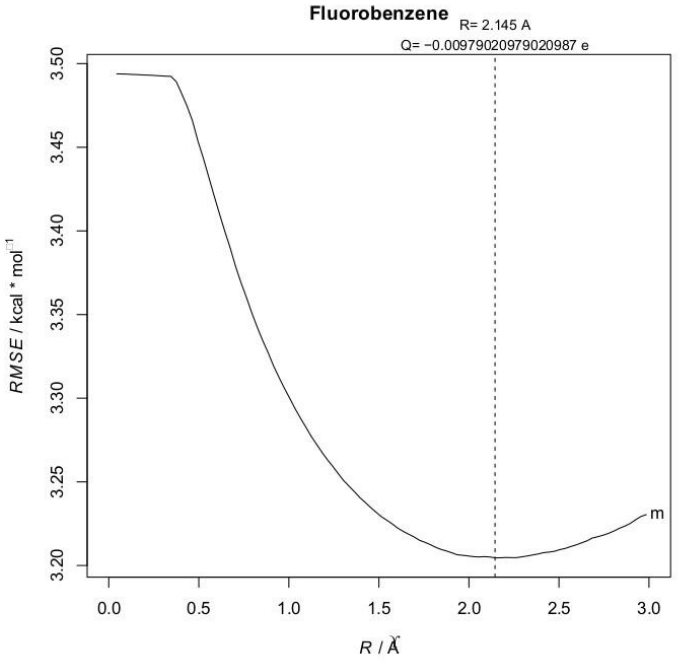


Finding Possible Use Cases: Heterocycles



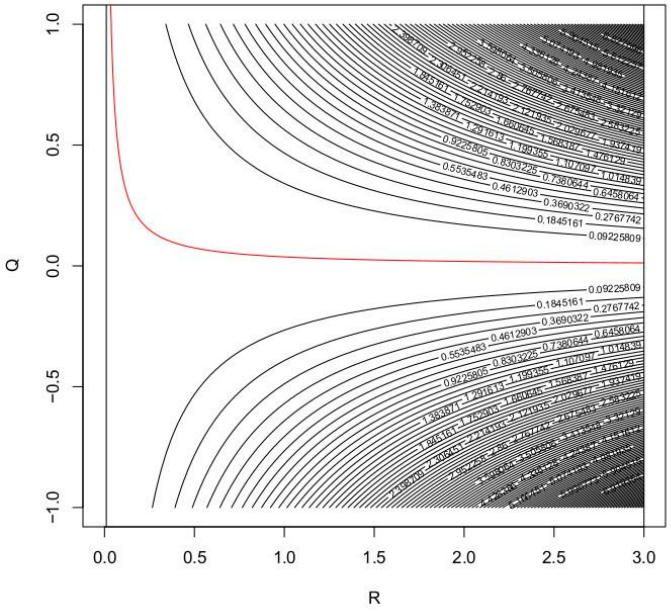
Dipole Error and ESP Error Minimization Deliver Reasonable Parameter Estimates

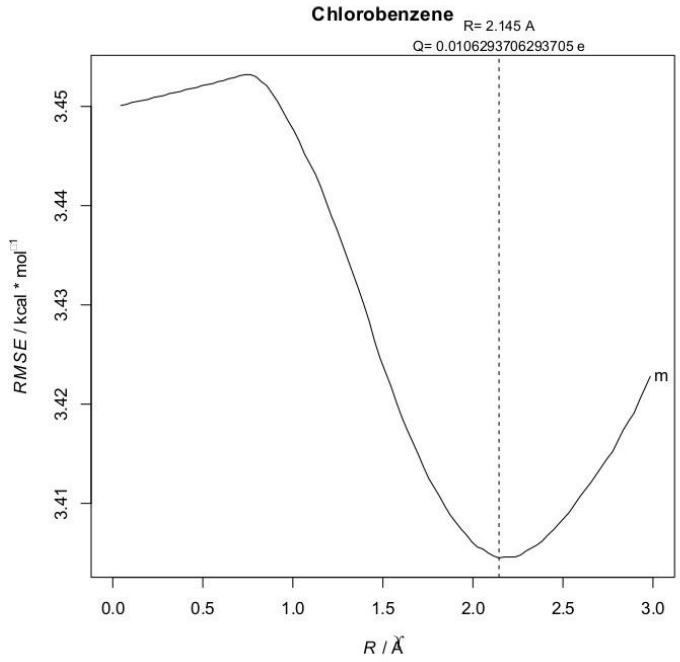




- No σ-hole, negative Off-Site Charge
- Lone pairs might be approachable in highly negative atoms

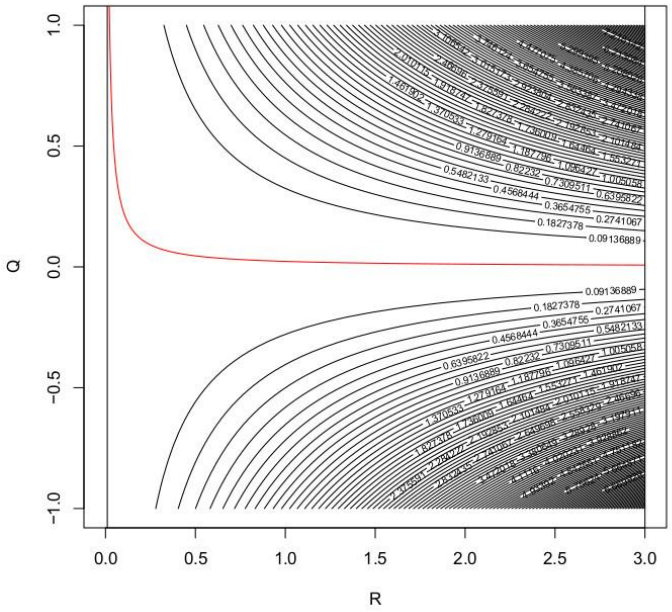
Dipole Error and ESP Error Minimization Deliver Reasonable Parameter Estimates

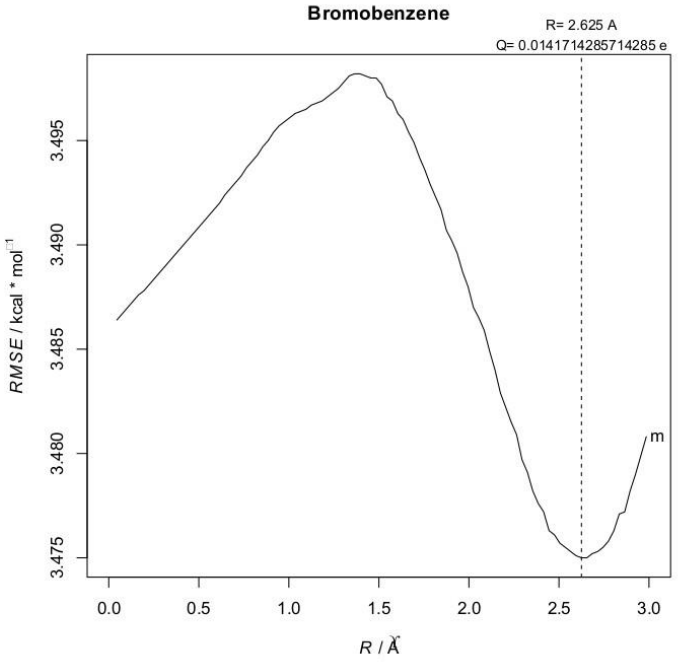




- σ-hole shows its effect
- Compatible with earlier parametrizations

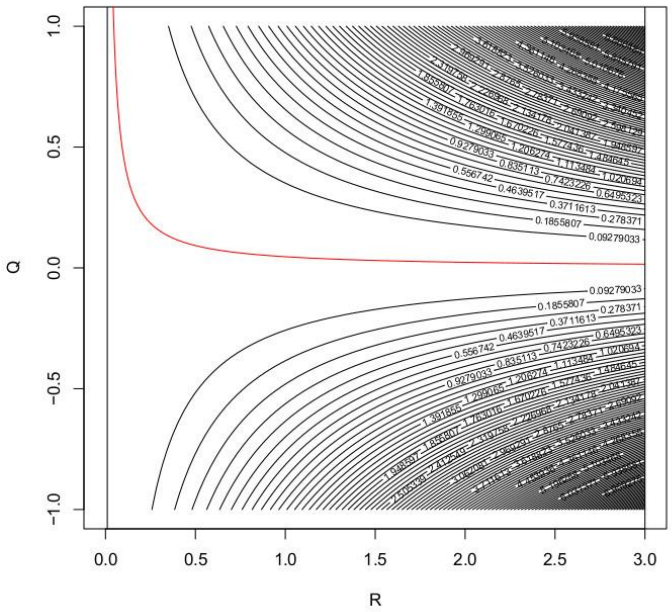
Dipole Error and ESP Error Minimization Deliver Reasonable Parameter Estimates

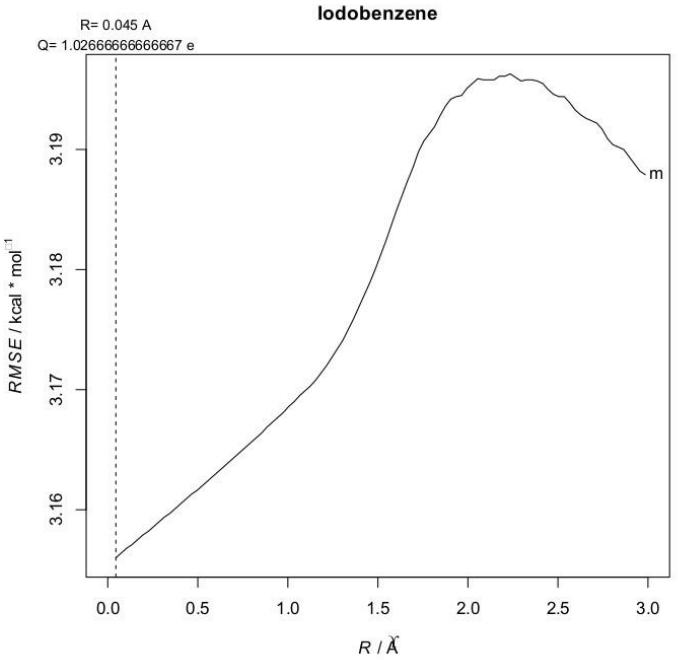




- Trend continues to follow the lower electronegativity
- Minima becomes less pronounced

Dipole Error and ESP Error Minimization Deliver Reasonable Parameter Estimates

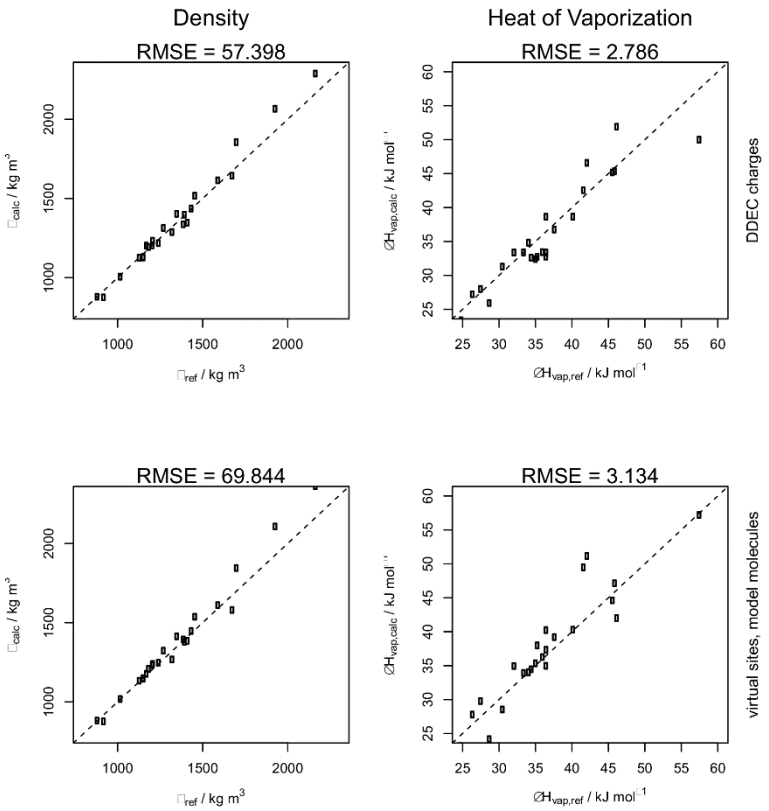




- No parameters found
- σ-hole is probably neutralized by EDG

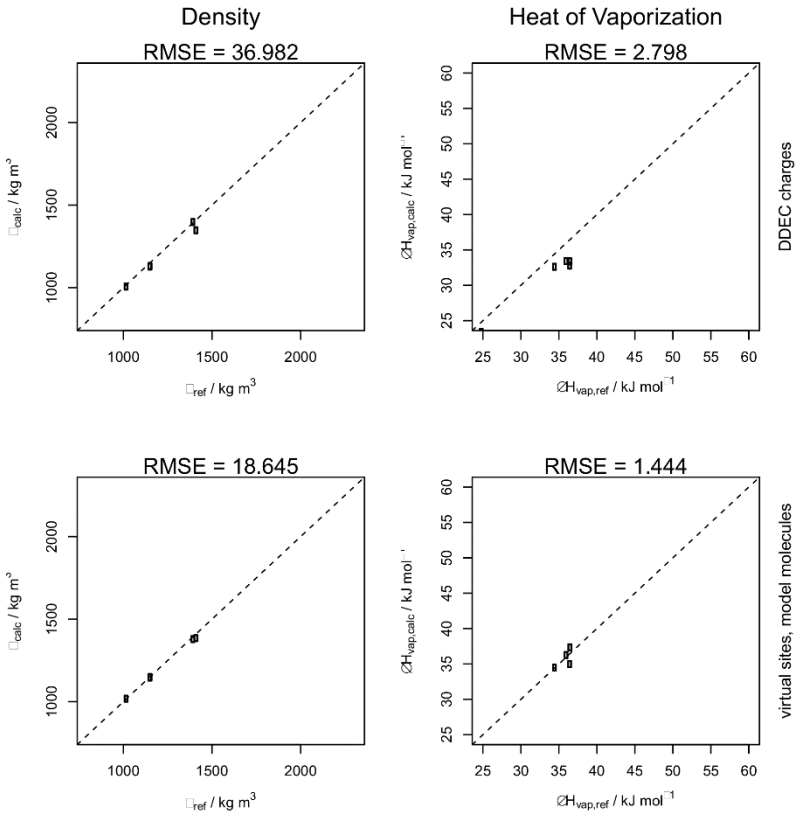
This Approach Limits Use Cases...

- Only molecules with a significant permanent dipole allow for sensible charge placement
- Many structures do not profit from individually computed parameters
- Parameters from reasonably similar model atoms often produced better results

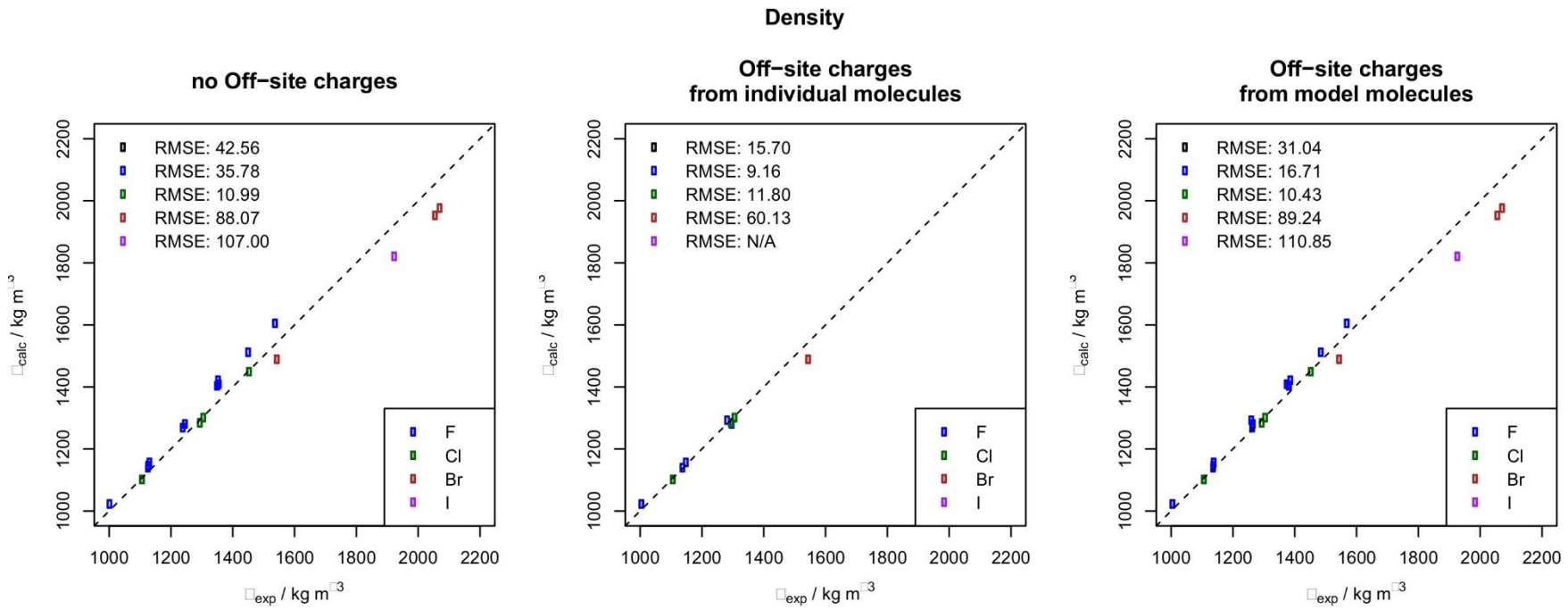


... But can help to Reproduce Liquid Properties in Small Molecules

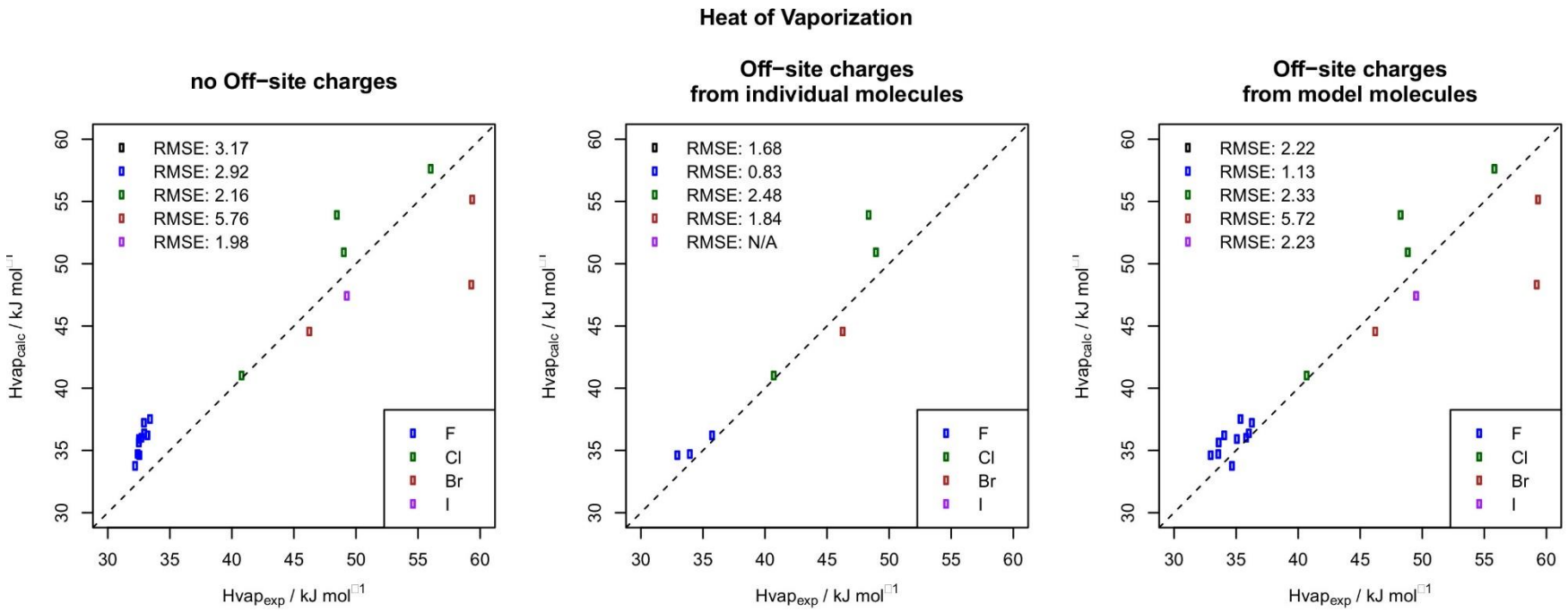
- A subset of Aryl halides showed significant improvements (-50% RMSE)
- But there are only 5 in the benchmark set
- So I made my own set



Application to Phenyl Halides



Application to Phenyl Halides



Conclusion

- Very good results for Aryl Fluorides
- Situational improvements for Aryl Chlorides and Bromides
- (probably) not applicable to Aryl Iodines

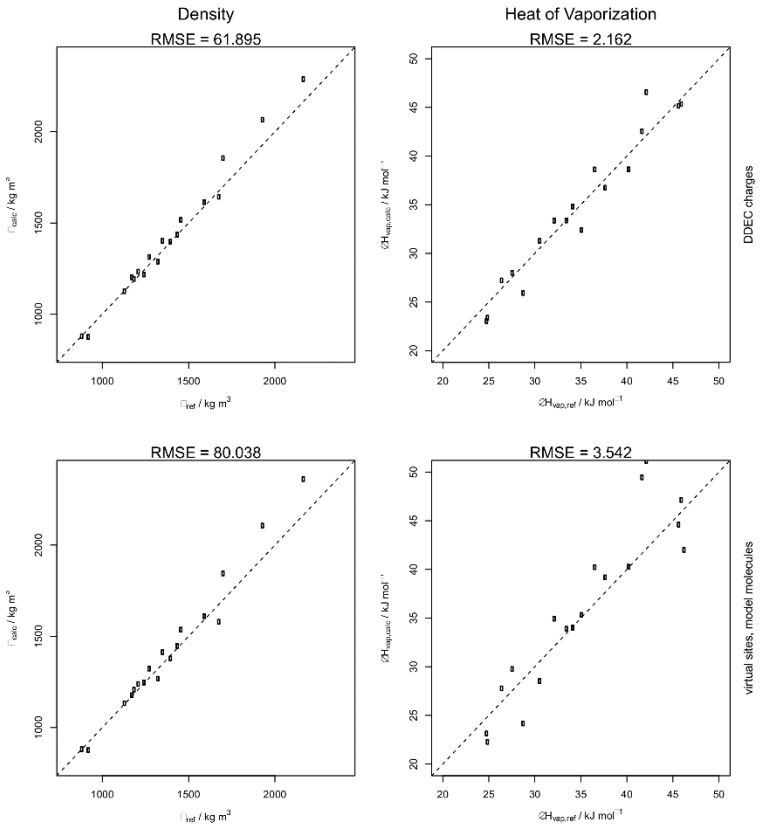
- Individual parametrization is often not worth the extra effort

- More practical: Use simple model molecules to determine parameters for large molecules

Advancing the Idea Beyond Phenyl Halides

- What about Alkyl Halides?

- Can we find similar approaches to...
  - Lone pairs?
  - Multiple bonds?



Questions?

Thank You For Everything!

Sources

- Kramer et al.; *J. Chem. Theory Comput.*, 2014, 10 (10), pp 4488–4496
- Cole et al.; *J. Chem. Theory Comput.*, 2016, 12 (5), pp 2312–2323
- Harder et al.; *J. Chem. Theory Comput.*, 2016, 12 (1), pp 281–296
- Caleman et al.; *J. Chem. Theory Comput.*, 2012, 8 (1), pp 61–74

Software Citations

- Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.

Software Citations

- Humphrey, W., Dalke, A. and Schulten, K., "VMD - Visual Molecular Dynamics", J. Molec. Graphics, 1996, vol. 14, pp. 33-38. URL http://www.ks.uiuc.edu/Research/vmd/
- R Core Team (2017). R: A language and environment for statistical computing. R Foundation for Statistical computing, Vienna, Austria. URL https://www.R-project.org/.
- MATLAB and Statistics Toolbox Release 2015a, The MathWorks, Inc., Natick, Massachusetts, United States.
- D. van der Spoel, E. Lindahl, B. Hess, and the GROMACS development team, GROMACS User Manual version 4.6.7, www.gromacs.org (2014)