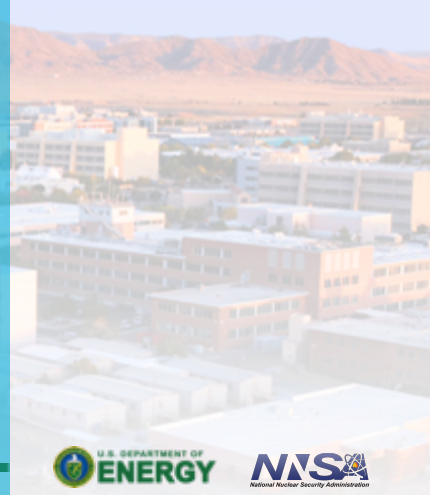
What can you do with a polarizable force field?

LAMMPS Workshop; August 2021

Joshua A. Rackers, Truman Fellow

Sandia National Laboratories



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Who am I?

Physics and Political Philosophy

High School Physics and Chemistry

Biophysics Ph.D.

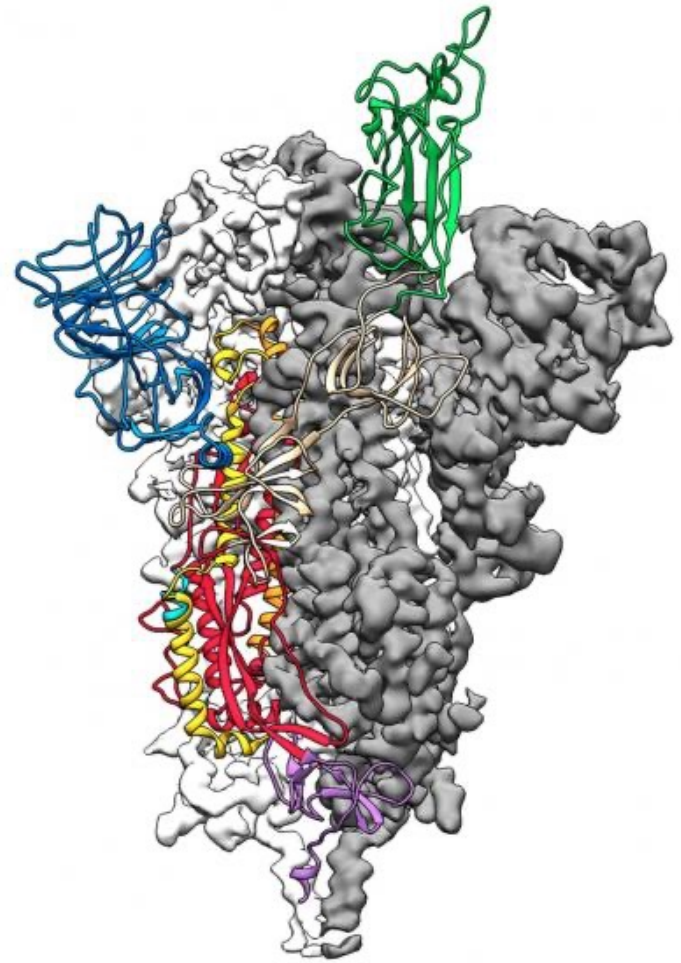
Truman Fellowship

The Grand Challenge of Molecular Science

Can we predict the behavior of molecules at the atomic scale?

$$F = ma$$

$$H\Psi = E\Psi$$



The Standard: Point Charge Force Field

$$U = \sum \tfrac{1}{2} K_b (b - b_0)^2 + \sum \tfrac{1}{2} K_\theta (\theta - \theta_0)^2$$

All Bonds — All Angles

$$+ \sum K_\phi [1 - \cos(n\phi + \delta)]$$

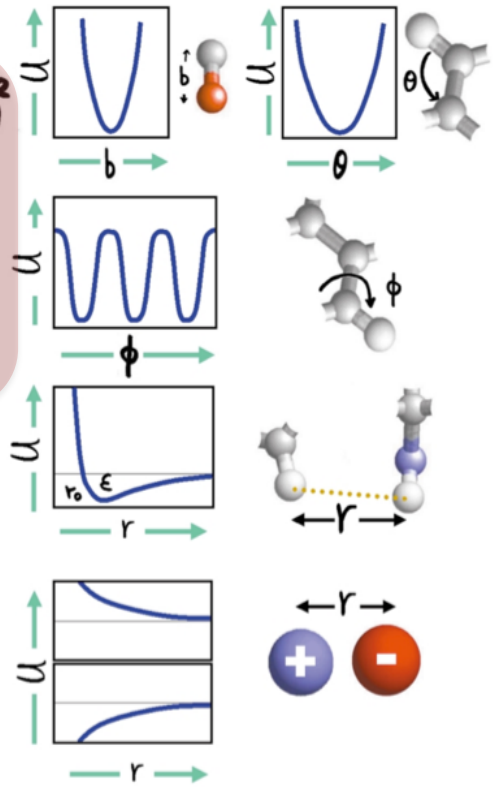
All Torsion Angles

$$+ \sum \varepsilon \left[\left(\frac{r_0}{r}\right)^{12} - 2\left(\frac{r_0}{r}\right)^{6} \right]$$

All nonbonded pairs

$$+ \sum 332 q_i q_j / r$$

All partial charges



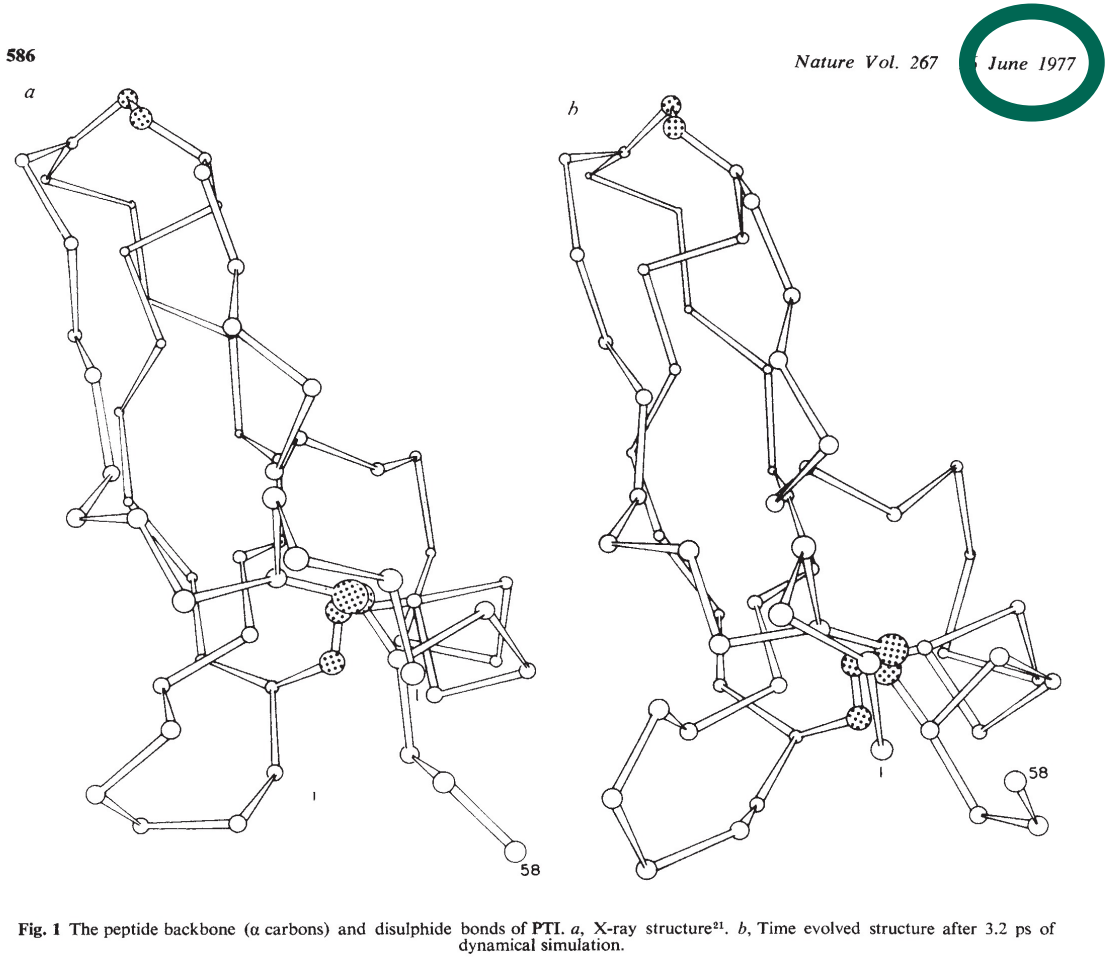
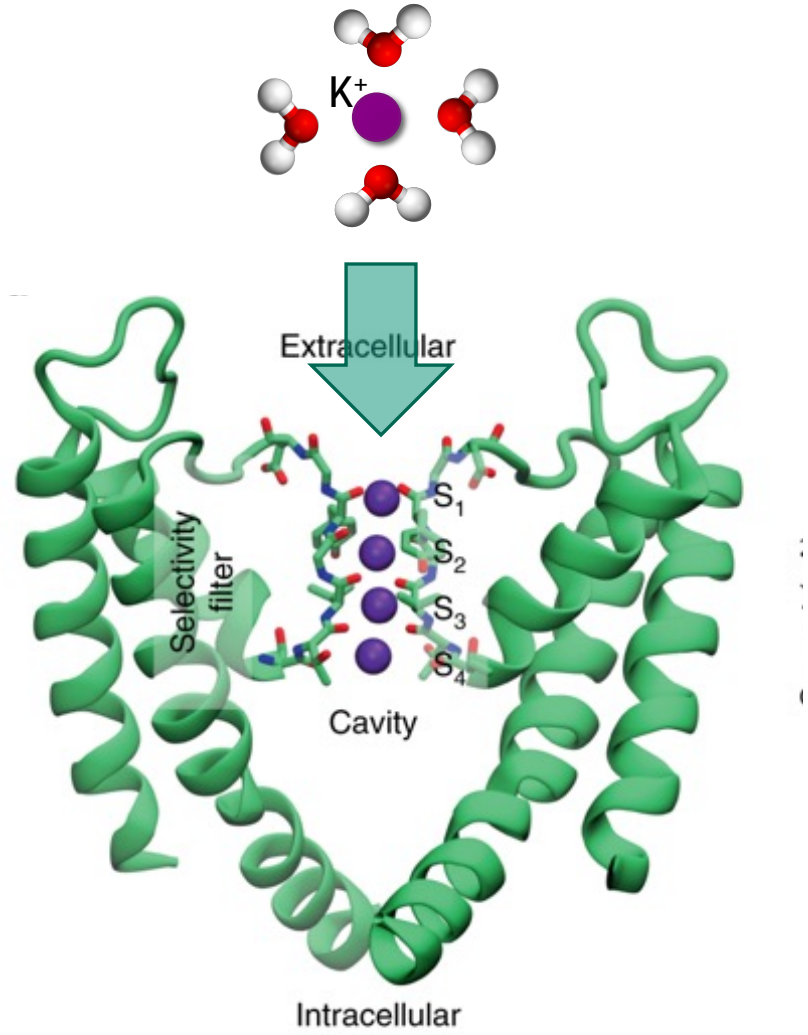


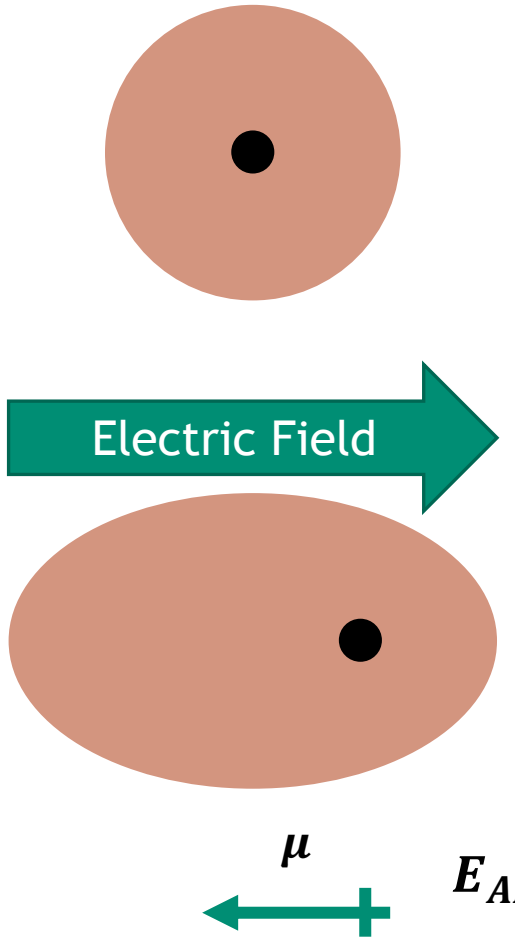
Fig. 1 The peptide backbone (α carbons) and disulphide bonds of PTI. *a*, X-ray structure[21]. *b*, Time evolved structure after 3.2 ps of dynamical simulation.

Atoms respond to their environment

Example: Ion Channel

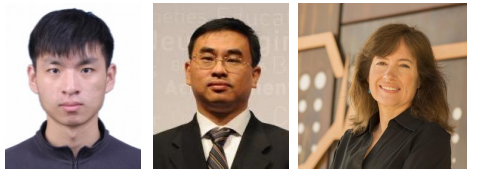


AMOEBA has induced dipoles

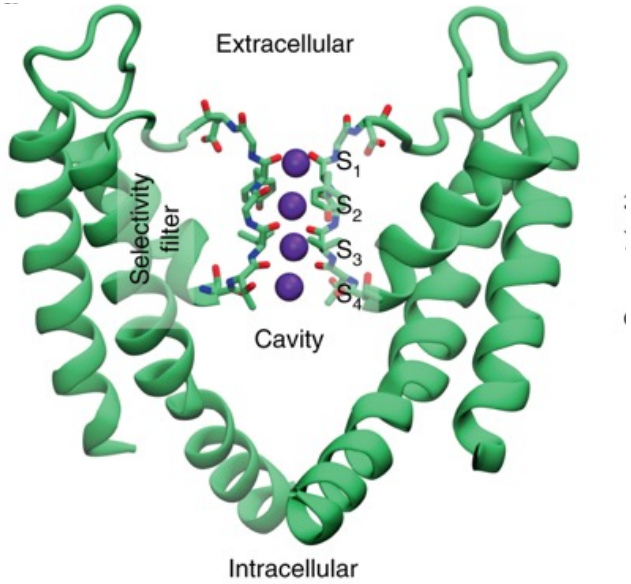


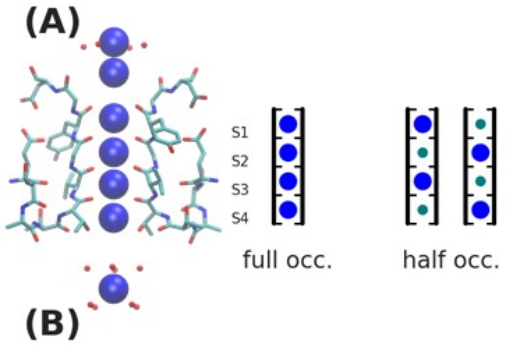
$$E_{AMOEBA} = E_{pair} + E_{pol}$$

AMOEBA Simulations of KcsA

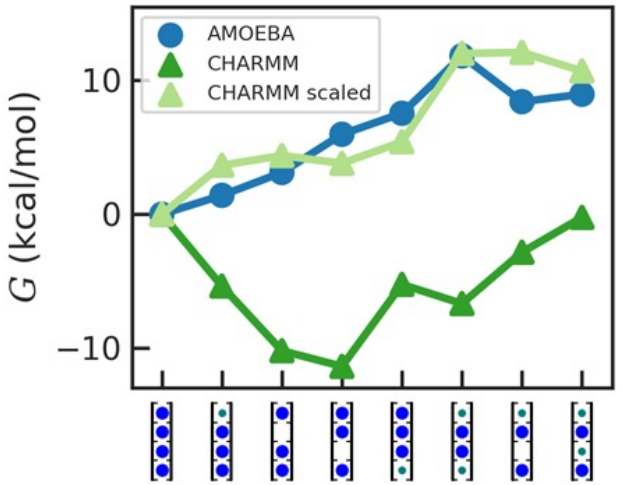


Is there water in the channel or not?

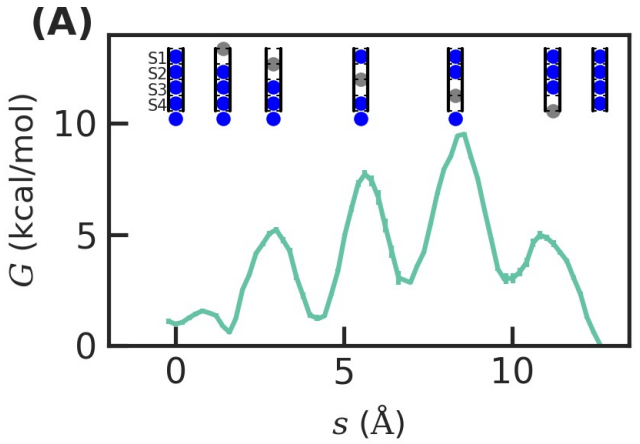




4 ions is most stable



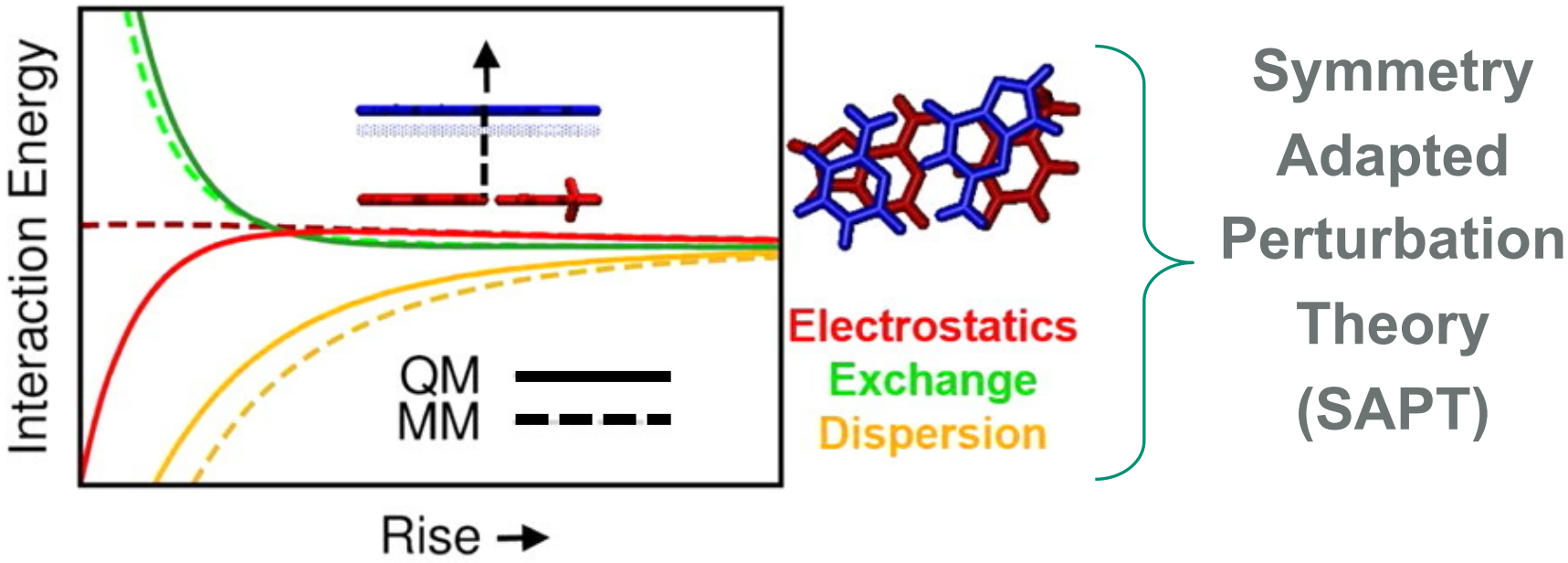
The free energy profile is consistent

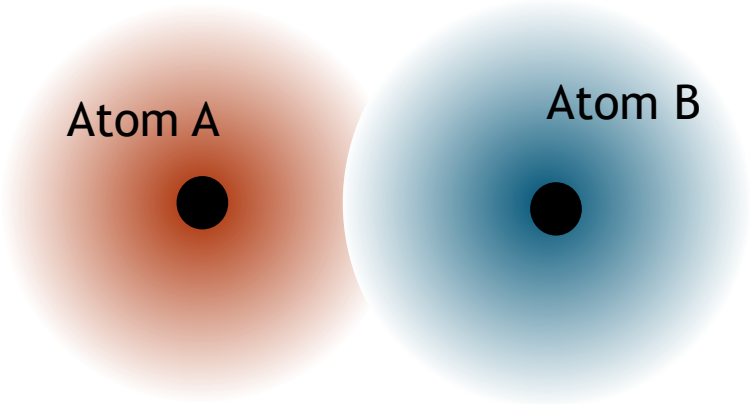


AMOEBA predicts no water in the channel

Jing, Rackers, et al. Chemical Science, 2021

AMOEBA still has errors because it is point-based

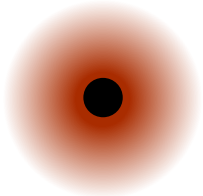




HIPPO: Hydrogen-Like Intermolecular Polarizable Potential

Point Force Fields

HIPPO



$U_{intermolecular}$ =

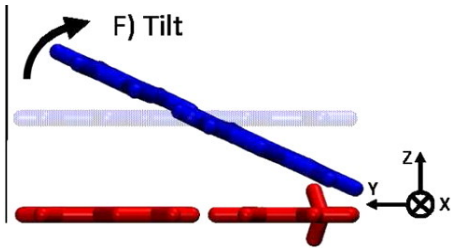
ab initio SAPT

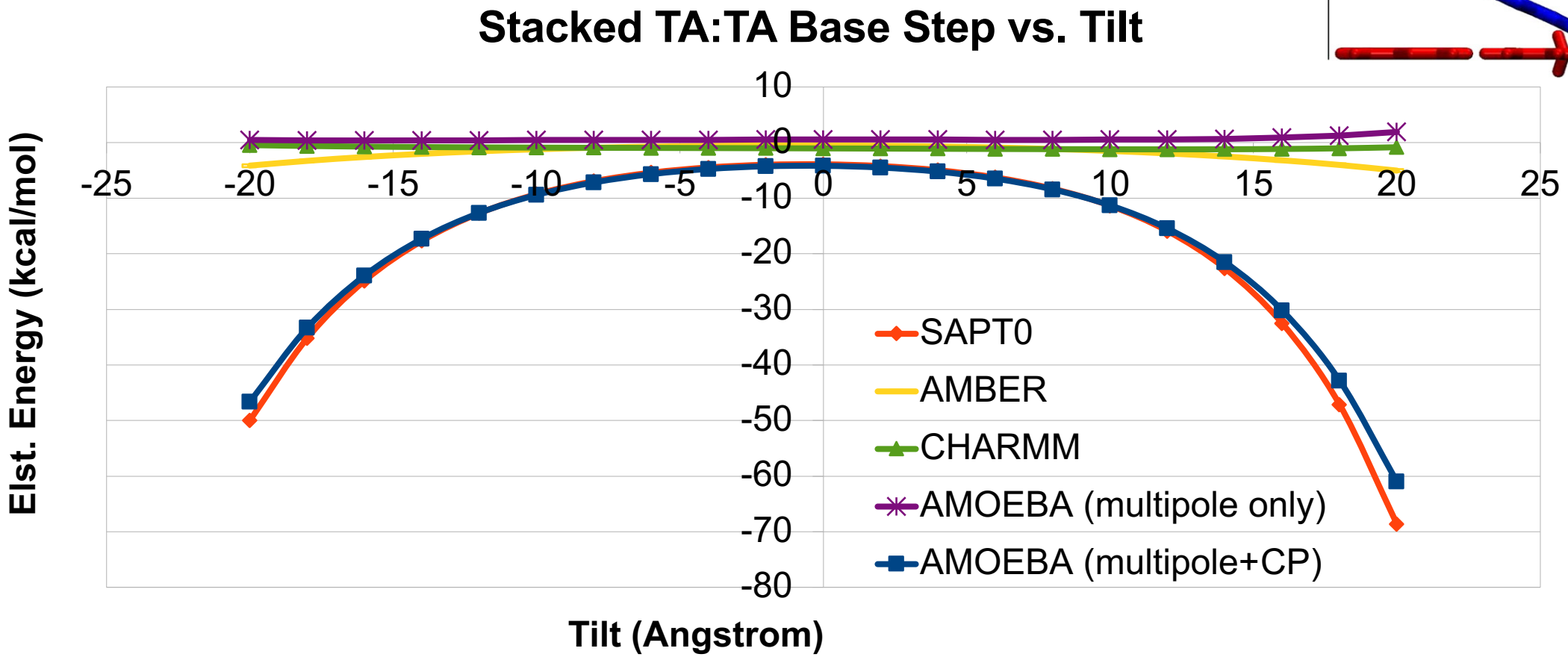
Electrostatics + Polarization +

Dispersion + Pauli Repulsion

HIPPO: Hydrogen-Like Intermolecular Polarizable Potential

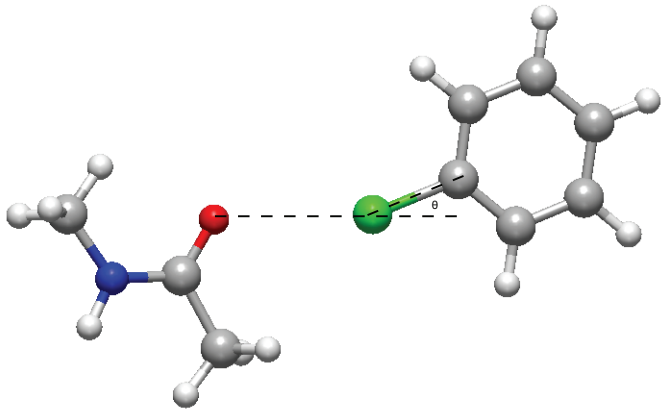
HIPPO gets base stacking right.

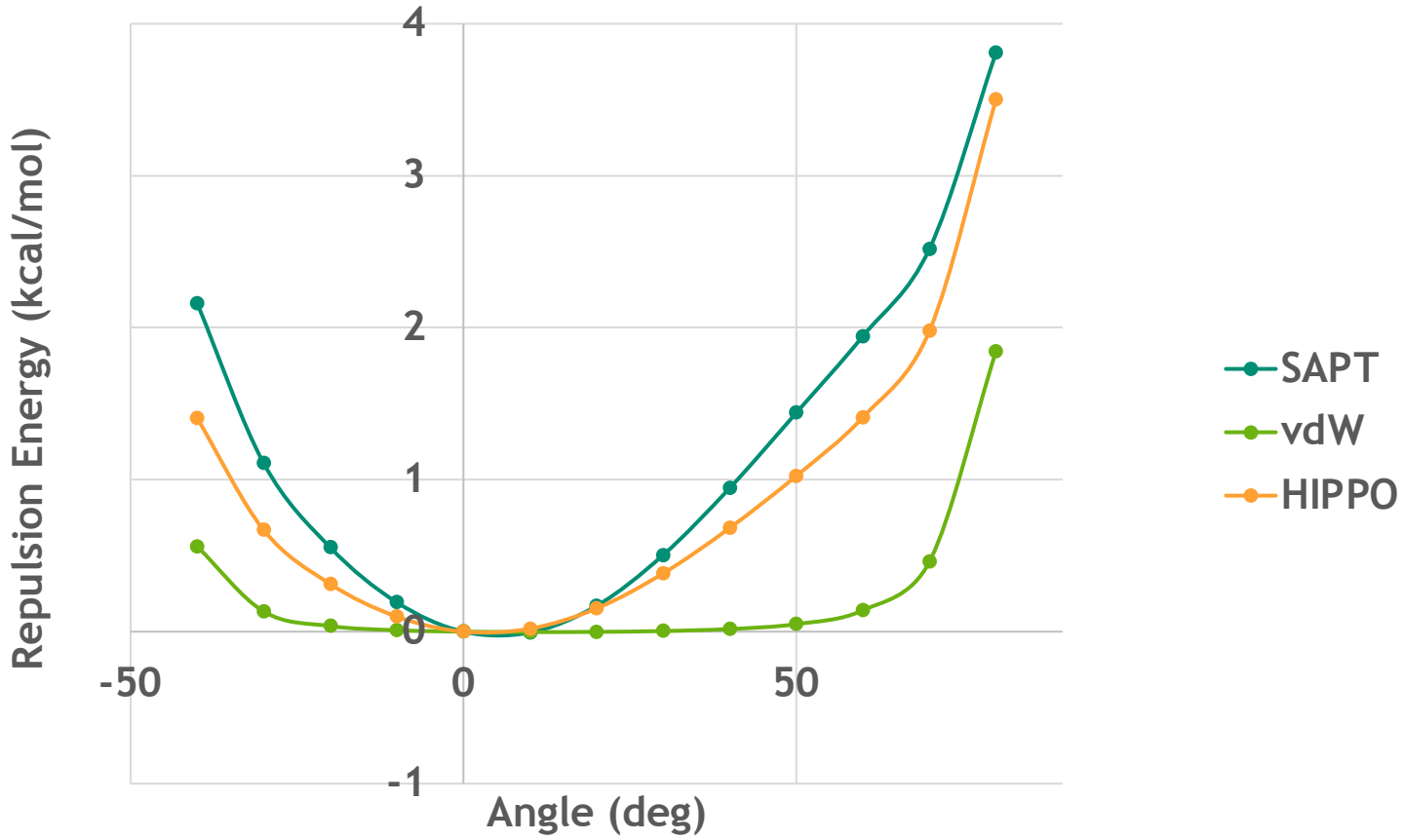




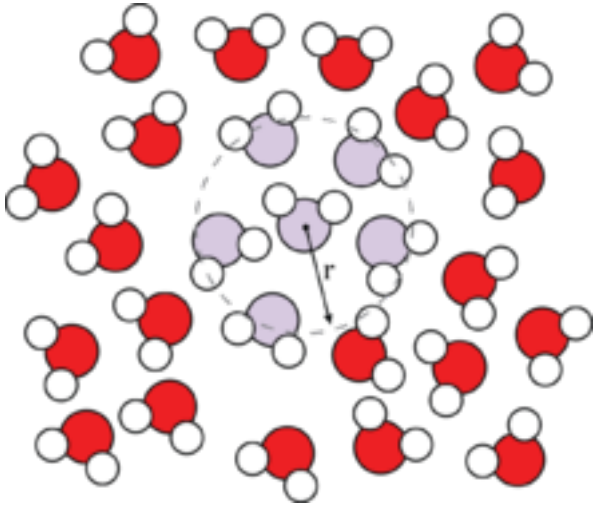
HIPPO: Hydrogen-Like Intermolecular Polarizable Potential

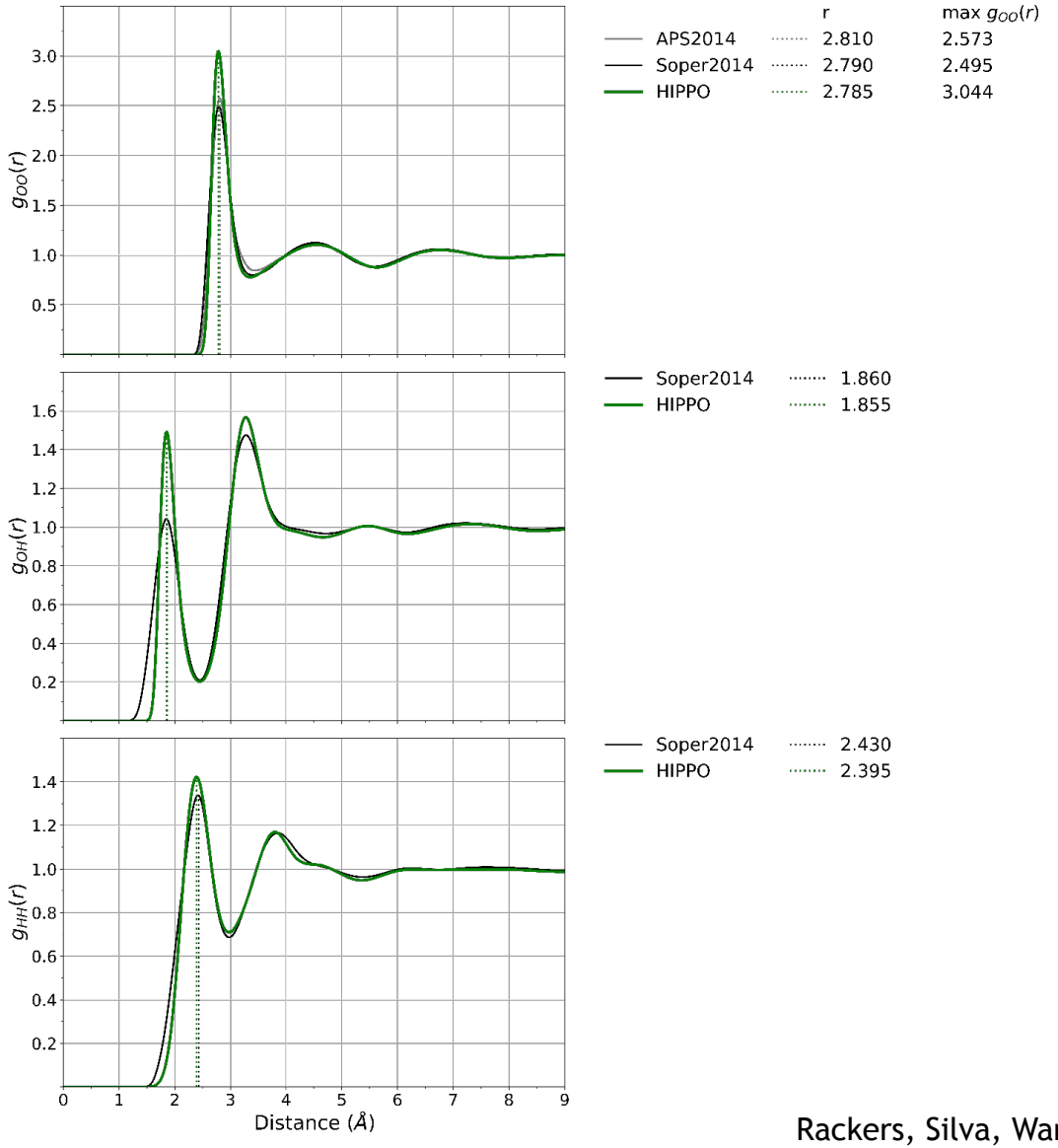
HIPPO gets drug binding interactions right.

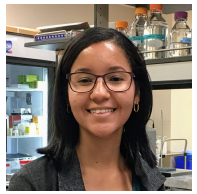


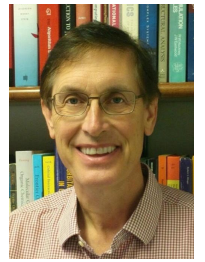


The HIPPO water model – Radial Distribution function





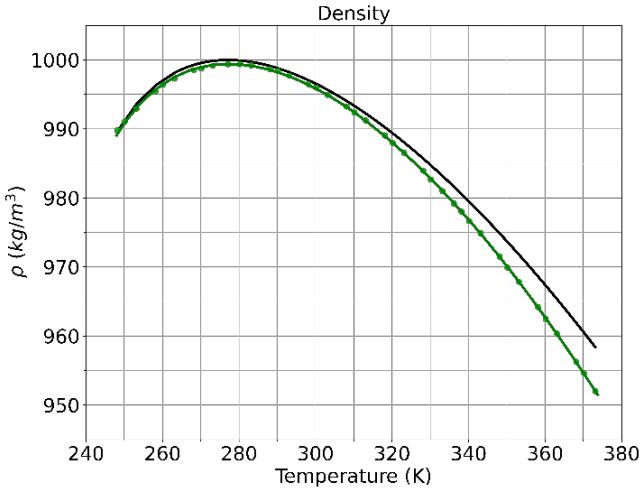




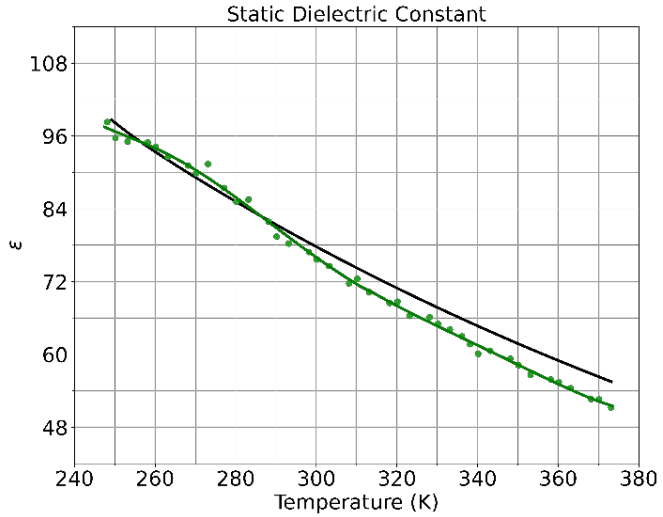
Rackers, Silva, Wang and Ponder, ArXiv 2021

The HIPPO water model – Temperature Dependence

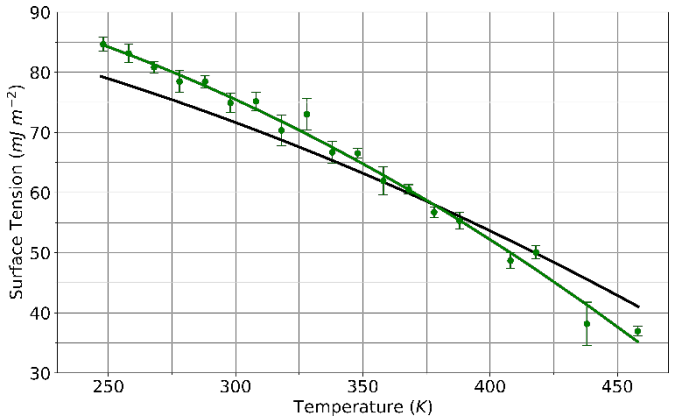
Density vs. Temperature



Dielectric Constant vs. Temperature

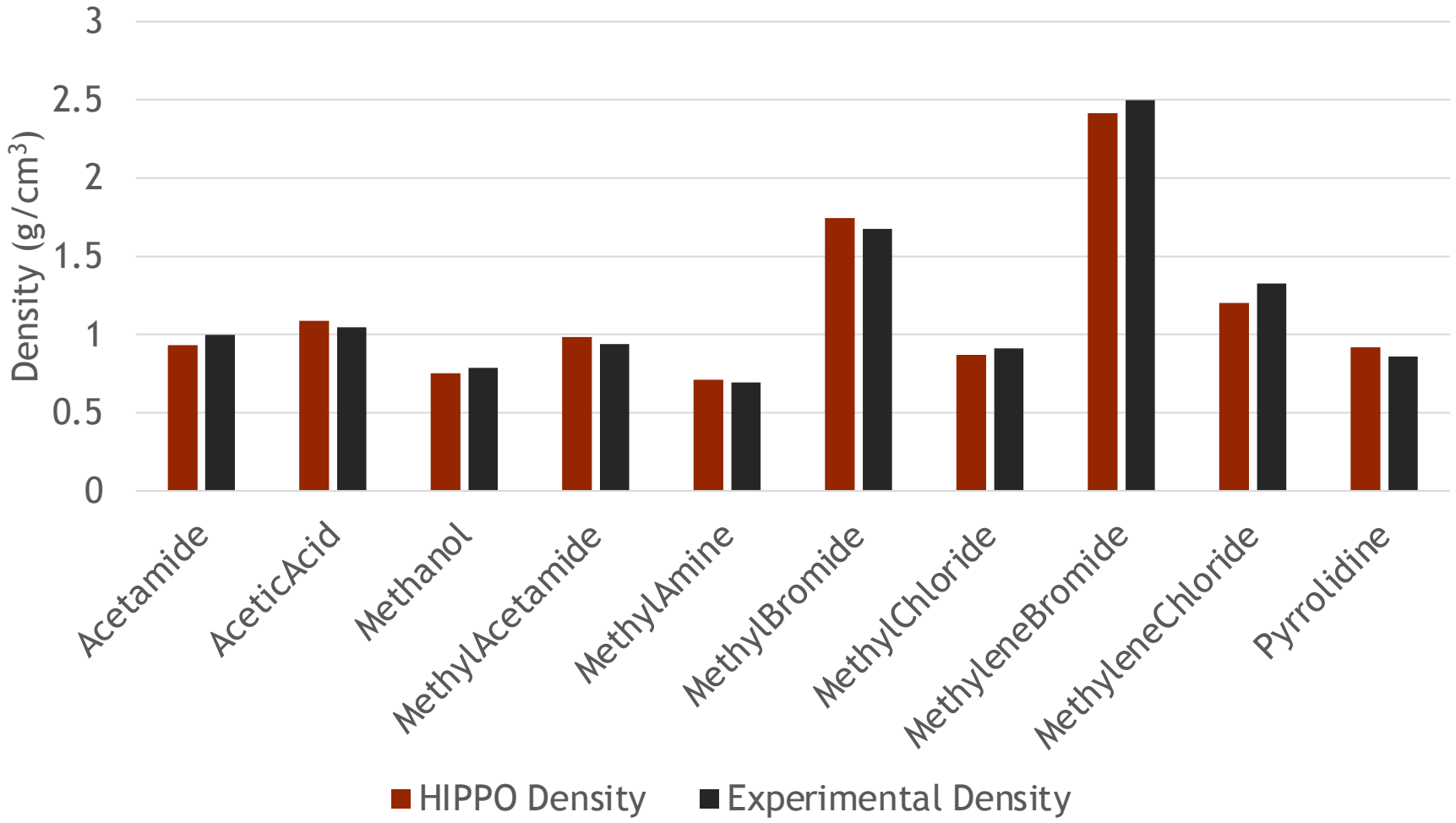


Surface Tension vs. Temperature



Rackers, Silva, Wang and Ponder, ArXiv 2021

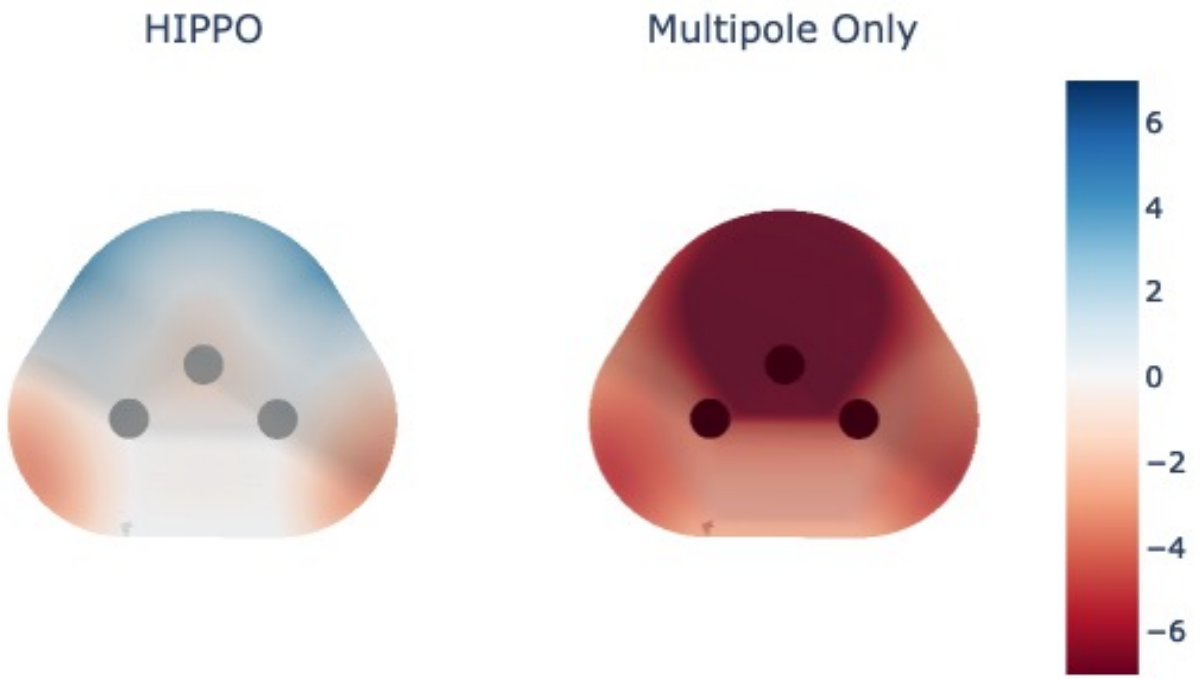
HIPPO for small molecules - preliminary



Why is HIPPO more accurate?

HIPPO is a closer approximation of intermolecular physics than any preceding Biomolecular Force Field.

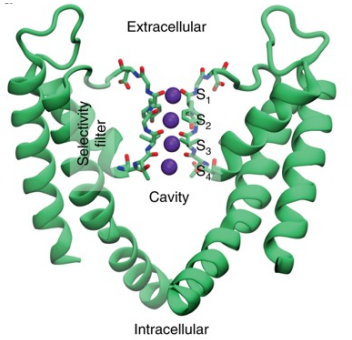
Electrostatic Potential Error at the vdW surface



Outlook

AMOEBA

- Polarization can give accurate protein simulations.
- We have done the first AMOEBA ion channel predictions.

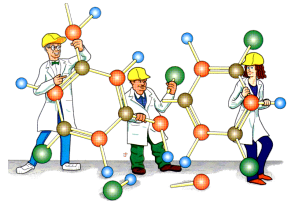


HIPPO

- Corrects the error(s) due to point approximation.
- Closely follows quantum mechanics.
- Produces very accurate model for water. Protein model soon.

Code

- AMOEBA/HIPPO presently available for GPUs on Tinker9 and OpenMM.
- AMOEBA/HIPPO coming to a LAMMPS release very soon!



OpenMM

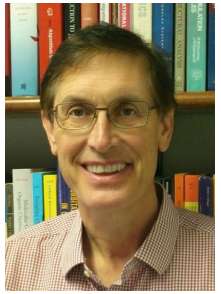
LAMMPS

Acknowledgements

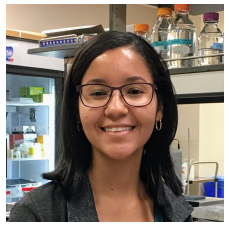
Steve Plimpton

Aidan Thompson

Susan Rempe



Jay Ponder



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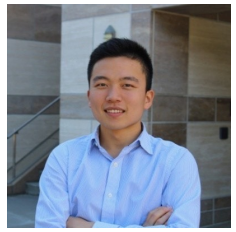

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