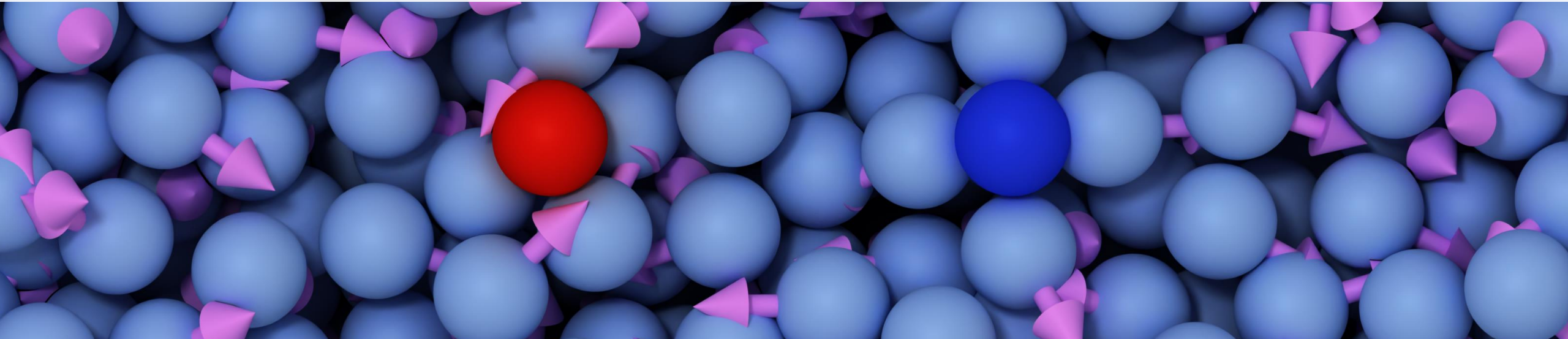
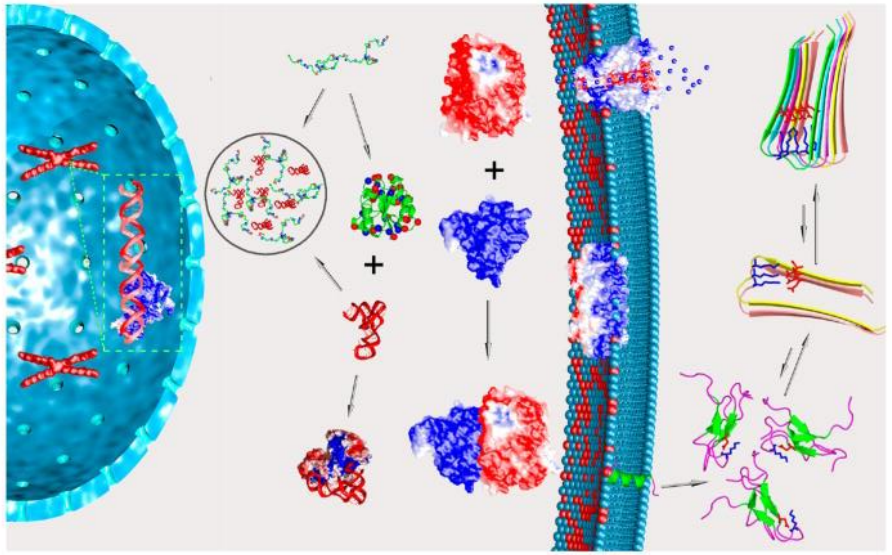
Unraveling Electrostatic Interactions in Dipolar Solvents

Christopher Balzer

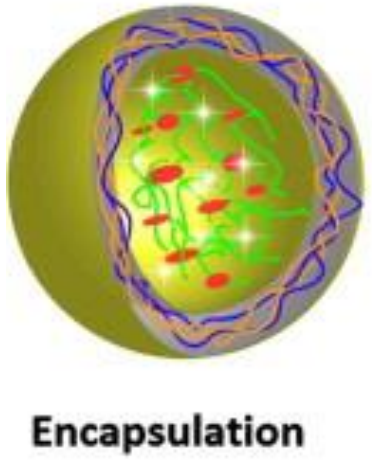
Varner, Balzer, Wang. *J. Phys. Chem. B* , 127, 19, 4328–4337, **2023**

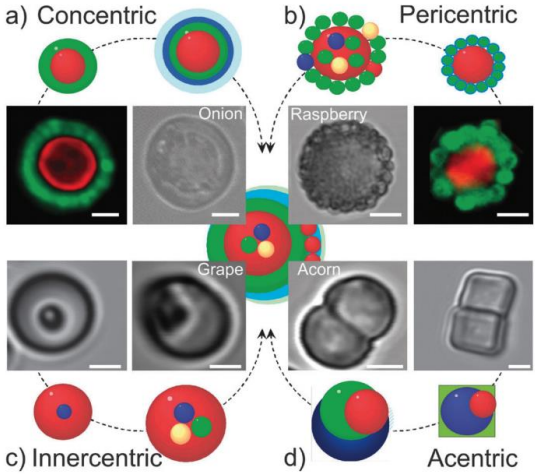


Electrostatic interactions help define our world



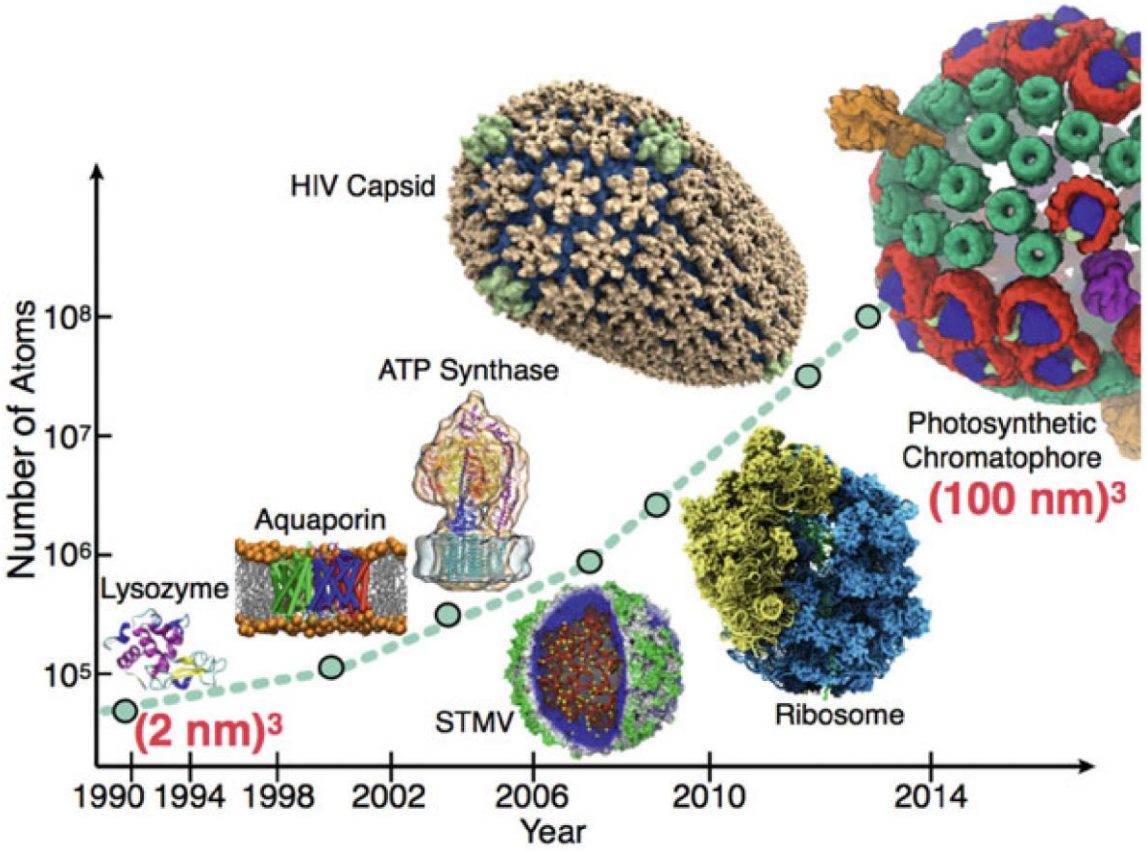
Zhou, Pang. *Chem Rev*., 118(4):1691-1741. **2018**



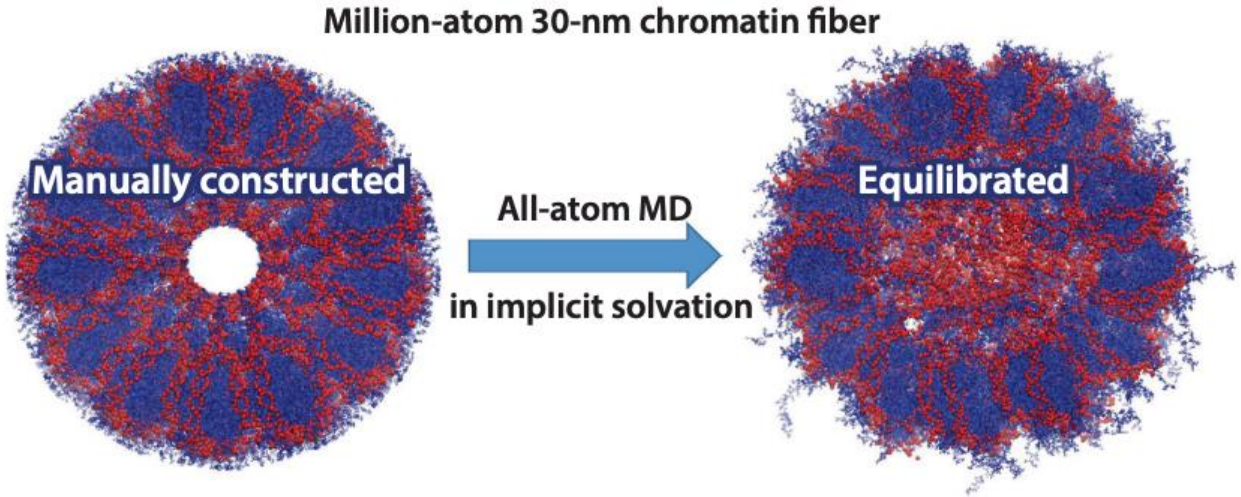


Yi and Sukhorukov. *Adv. in Coll. and Interface Sci.*, 207, 280-289. **2014**

Molecular dynamics in biophysical systems



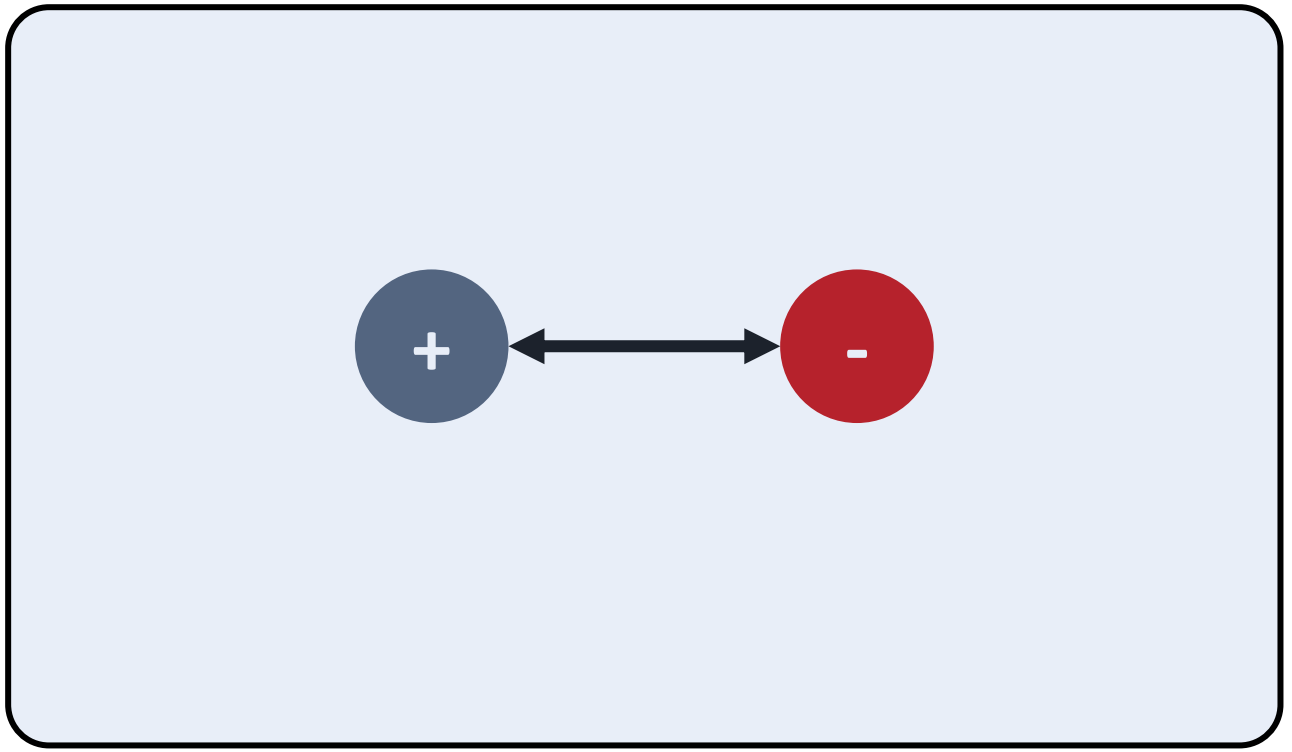
Wilson, E. *et al.*. Structure and Function of Membrane Proteins. Methods in Molecular Biology, **2021**



Onufriev and Case. *Annu. Rev. Biophys.* 48:275–96, **2019**

Today’s focus

The interaction between two oppositely charged ions

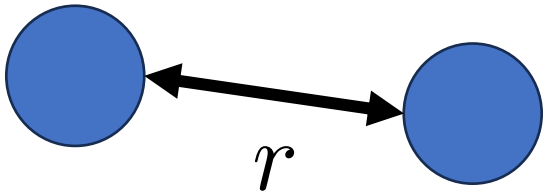


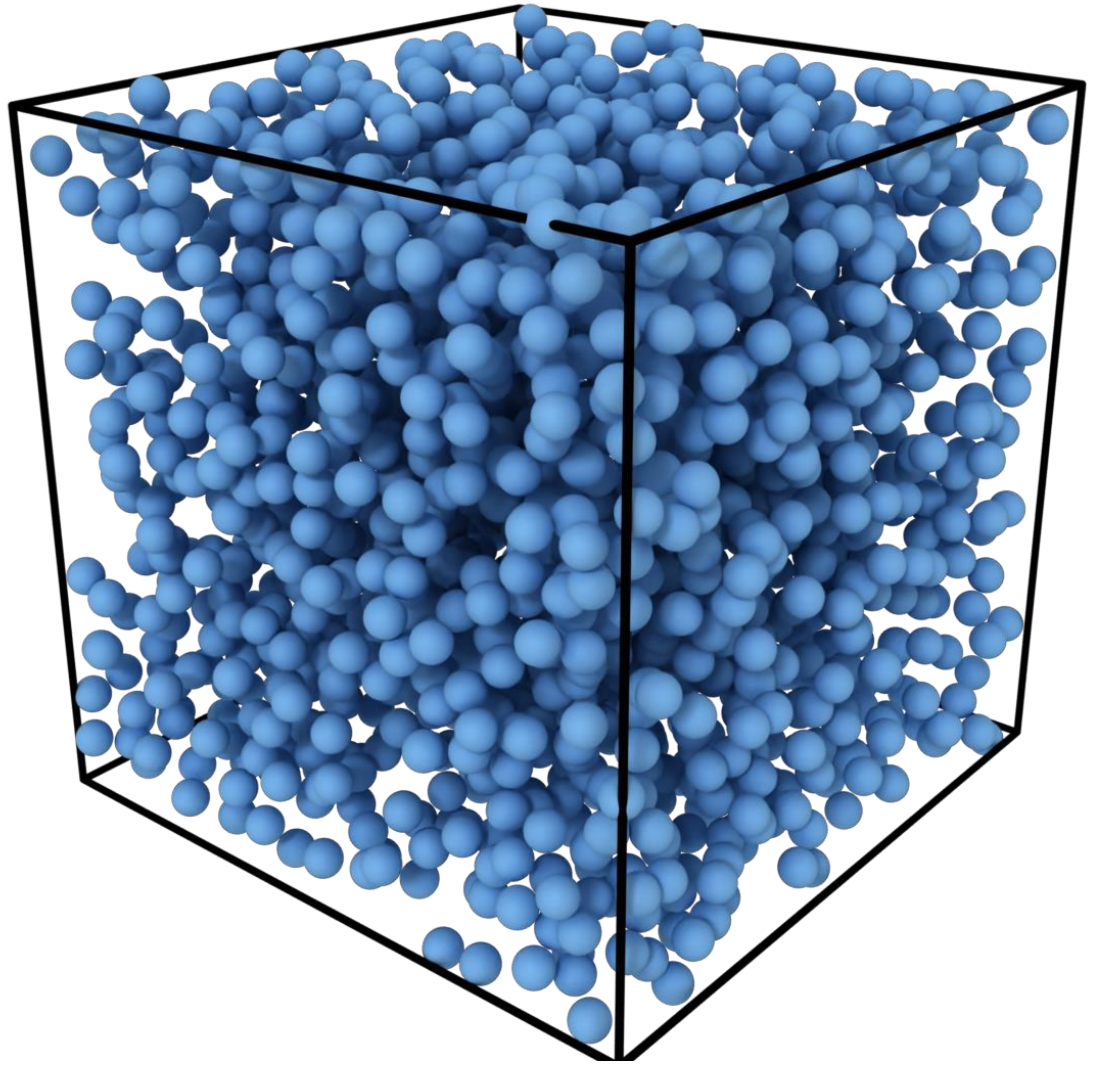
Molecular dynamics simulations

- Specify a pairwise potential between particles and evolve the system in time

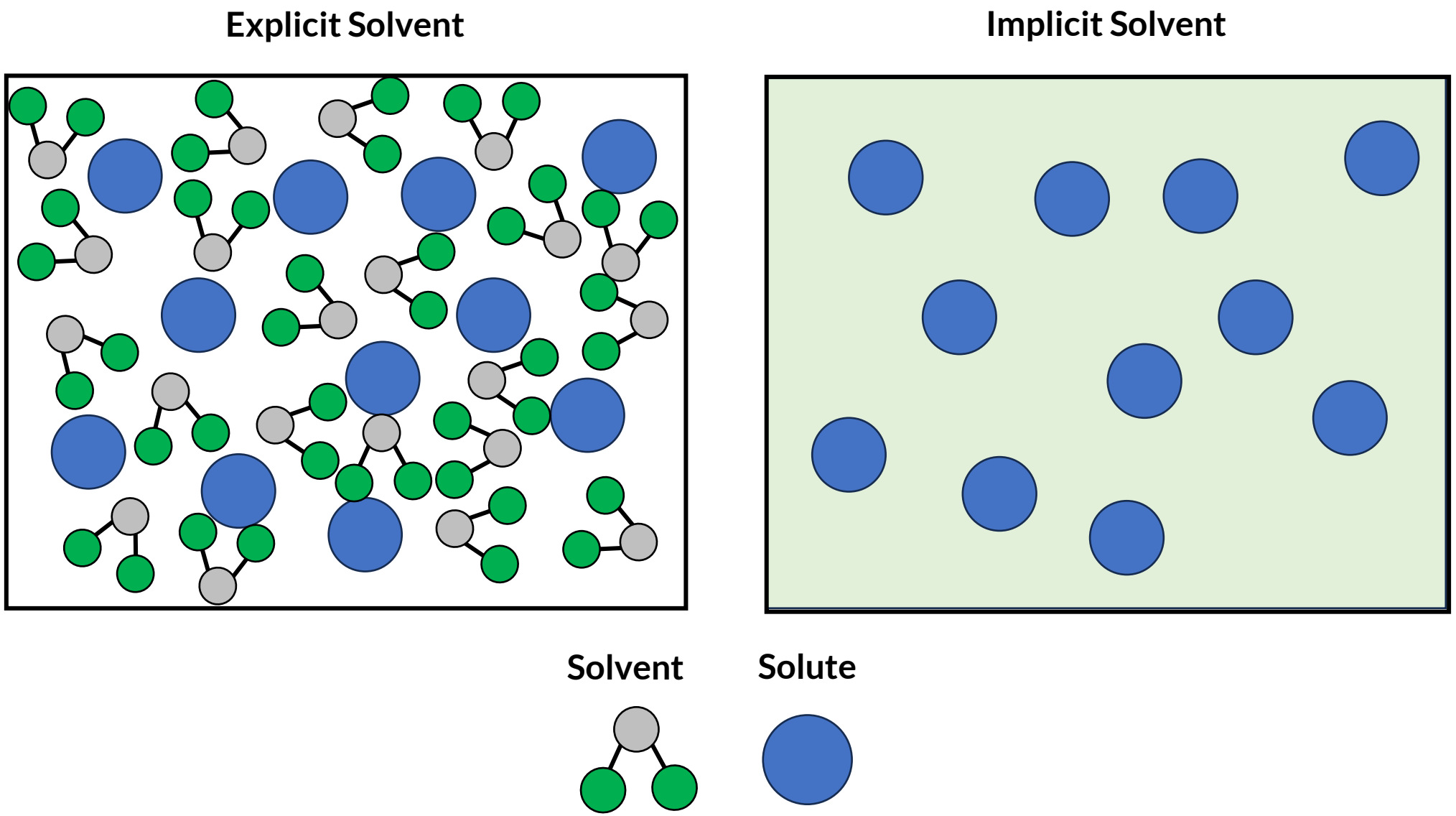
  Ex. Lennard-Jones fluid

$$U(r) = \left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}$$



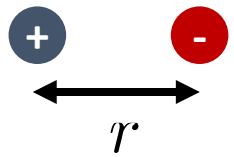


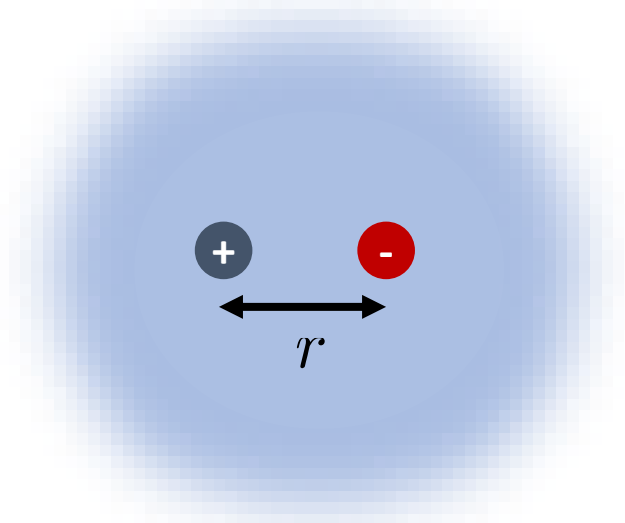
Implicit versus explicit solvent



Where do the degrees of freedom go?

- Solvent degrees of freedom are embedded into the dielectric constant





Vacuum

$$U(r) = \frac{-1}{4\pi\epsilon_0 r}$$

Dielectric Background

$$U(r) = \frac{-1}{4\pi\epsilon(\Theta) r}$$

Debye (1912)

$$\frac{\varepsilon - 1}{\varepsilon - 2} = \frac{\beta\rho\mu^2}{9}$$

Kirkwood-Fröhlich (1939)

$$\frac{(\varepsilon - 1)(2\varepsilon + 1)}{2\varepsilon} = \frac{\beta\rho\mu^2}{3}(1 + z\langle\cos\theta\rangle)$$

Debye, *Some Results of a Kinetic Theory of Insulators* (1912), Fröhlich, H. *Theory of Dielectrics*, 2nd ed. (1958)

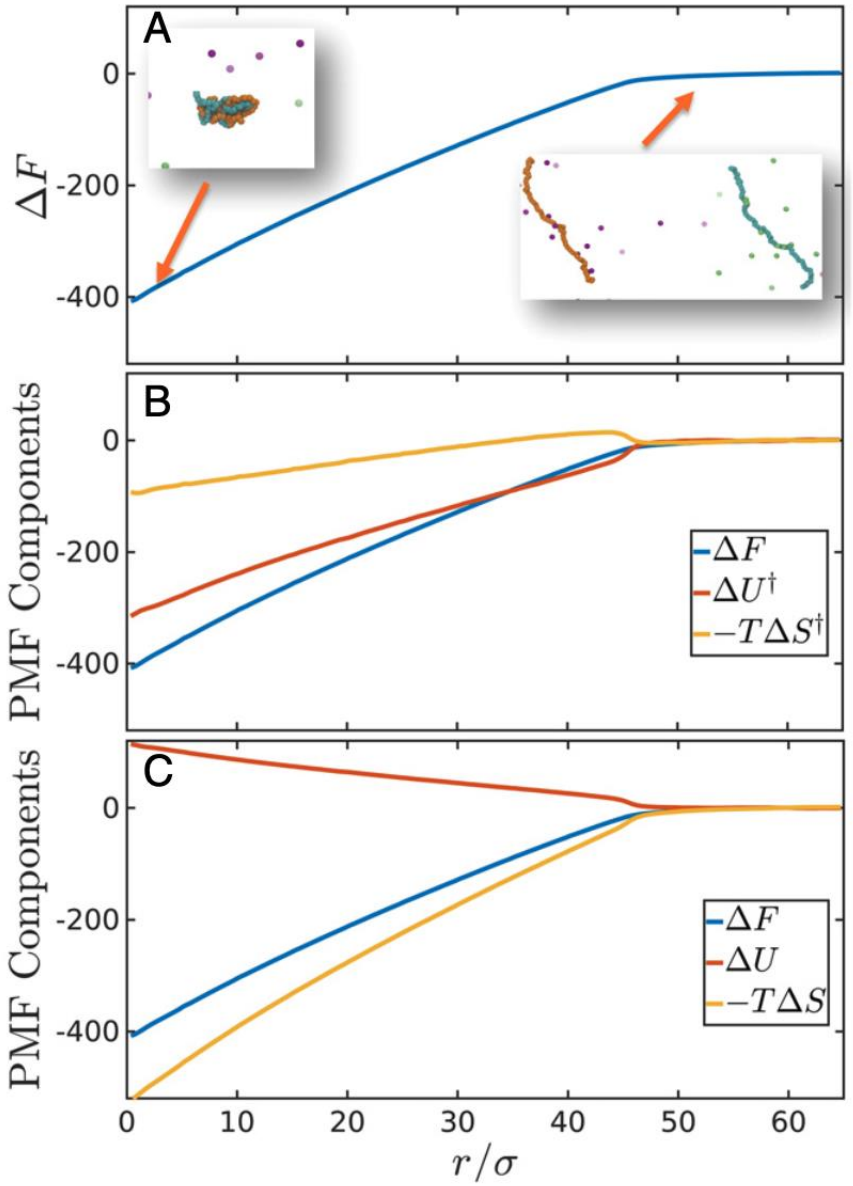
Consequence of implicit solvent potentials

- In implicit solvent models, the energy of a given microstate has a temperature dependence

$$F = -k_B\,T\ln(Z) = -k_B\,T\ln\left(\sum_{\Gamma} e^{-E[\Gamma]/k_B\,T}\right),$$

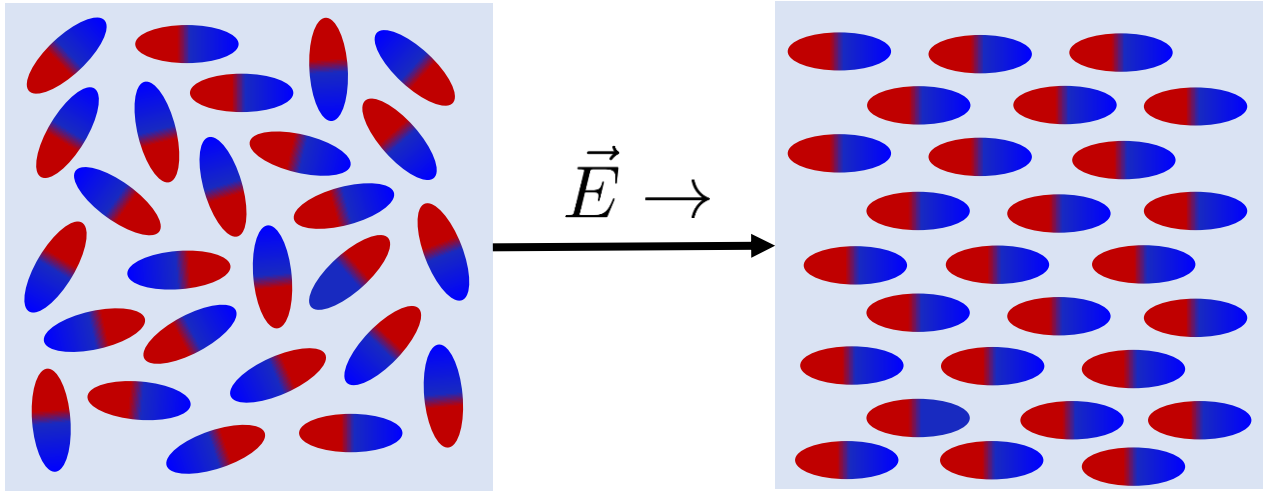
- Entropy is hidden in the energy's temperature dependence

$$-TS = F - \langle E\rangle + T\left\langle\frac{\partial E}{\partial T}\right\rangle.$$



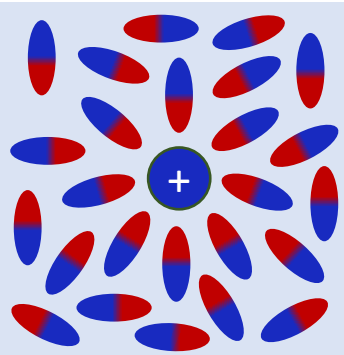
Chen and Wang. *PNAS*, 119 e2209975119 (2021)

Dipole orientation in the presence of fields

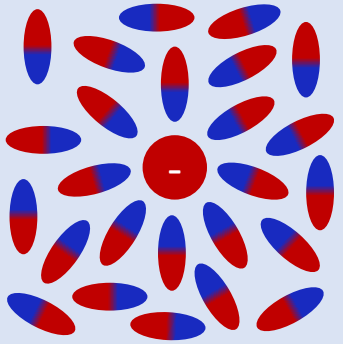


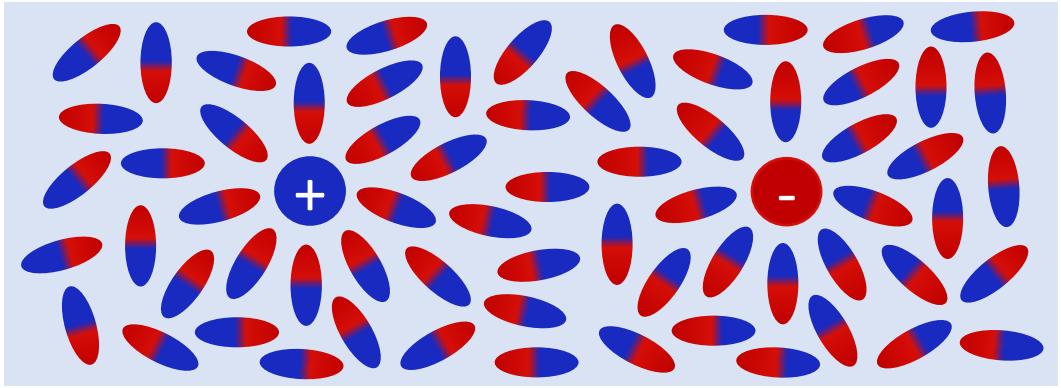
Charges generate an electric field → can be ions, charged macromolecules, etc.

A simple potential of mean force



Dipoles are random
far away from ions





$$\Delta F = \frac{q_i q_j}{4\pi\epsilon(\Theta) r} \qquad \text{(PMF)}$$

$$\Delta S = \frac{q_i q_j}{4\pi\epsilon(\Theta) r} \frac{\partial\epsilon(\Theta)}{\partial T}$$

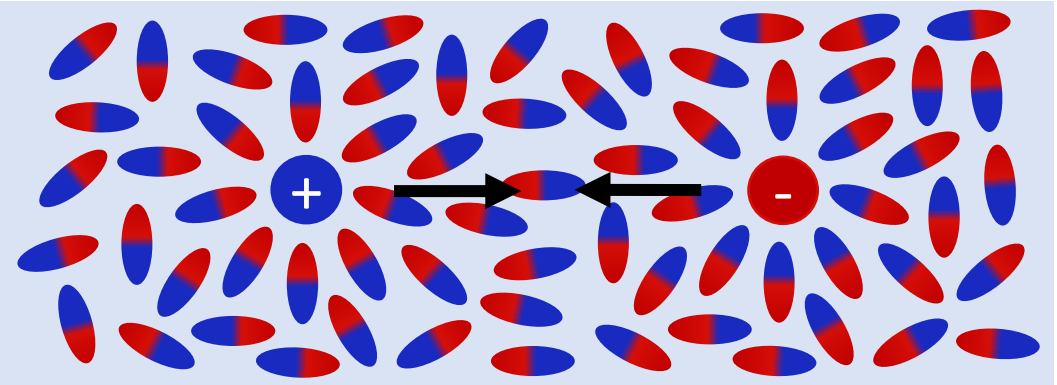
$$\Delta U = \Delta F + T\Delta S = \frac{q_i q_j}{4\pi\epsilon(\Theta) r} \left(1 + T\frac{\partial\epsilon(\Theta)}{\partial T}\right)$$

Motivating questions

1. How important is the electrostatic entropy in solvent mediated ionic interactions?
2. Under what conditions will entropy dominate the potential of mean force?
3. What is the underlying molecular picture?
4. Is this phenomenon general or solvent/ion specific?

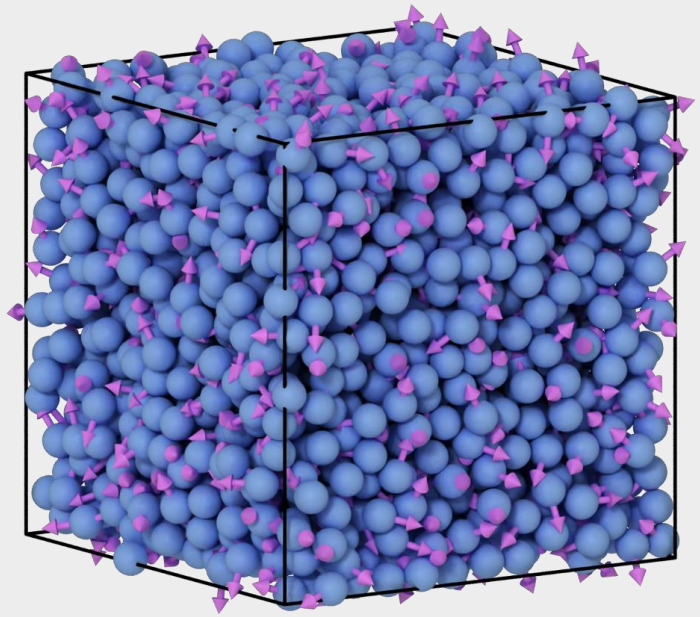
System and Methods

- Two oppositely charged ions immersed in a dipolar solvent

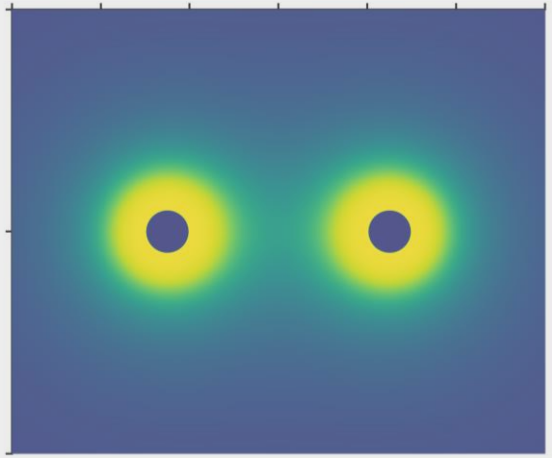


$$PMF \rightarrow \Delta F = \Delta U - T\Delta S$$

Coarse-grained molecular dynamics



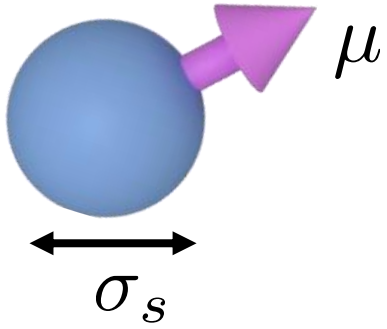
Dipolar Self-Consistent Field Theory



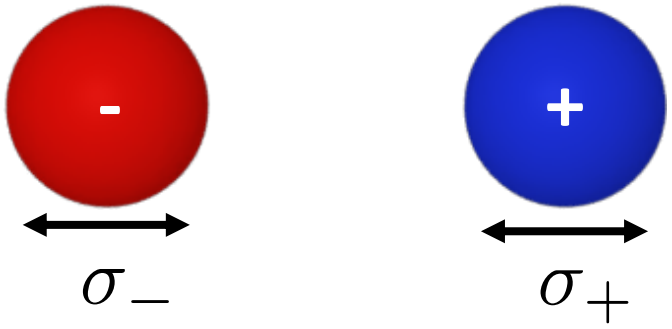
$$\Xi = \int \mathcal{D}w \int \mathcal{D}w_{\mathrm{or}} \int \mathcal{D}w_{\mathrm{el}} \int \mathcal{D}\rho_{\mathrm{or}} \int \mathcal{D}\rho_{\mathrm{el}}\, e^{-\beta H}$$

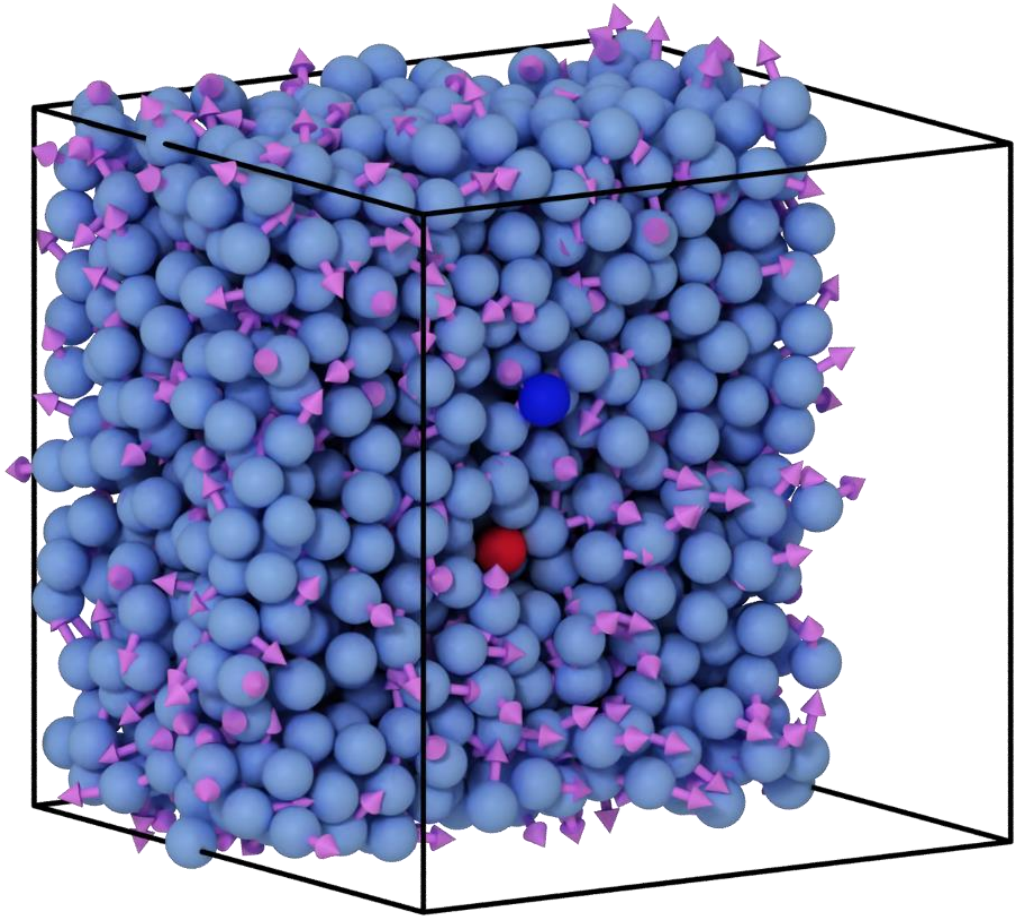
Ions in Stockmayer fluid

- Solvent beads are neutral with a point dipole



- Point charge at center of mass





Stockmayer fluid - Pair potentials

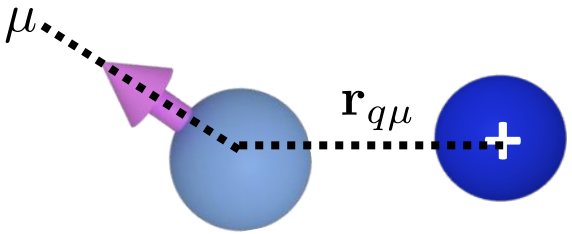
WCA Potential

$$U_{ij}^{LJ}(r) = \begin{cases} 4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r}\right)^{12} - \left(\frac{\sigma_{ij}}{r}\right)^{6} + \frac{1}{4}\right] & r \leq 2^{1/6}\sigma_{ij} \\ 0 & r > 2^{1/6}\sigma_{ij} \end{cases}$$

Charge-Charge

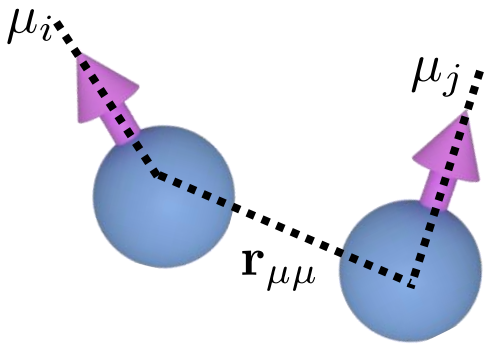
$$U_{ij}^{qq}(r) = \frac{1}{4\pi\varepsilon_0}\frac{q_i q_j}{r}$$

Charge-Dipole



$$U^{q\mu}(\mathbf{r}) = \frac{1}{4\pi\varepsilon_0}\frac{q(\mathbf{r}_{q\mu}\cdot\boldsymbol{\mu})}{|\mathbf{r}_{q\mu}|^3}$$

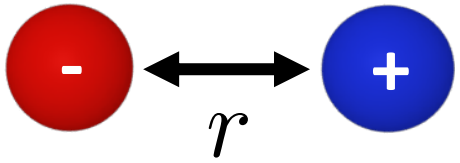
Dipole-Dipole



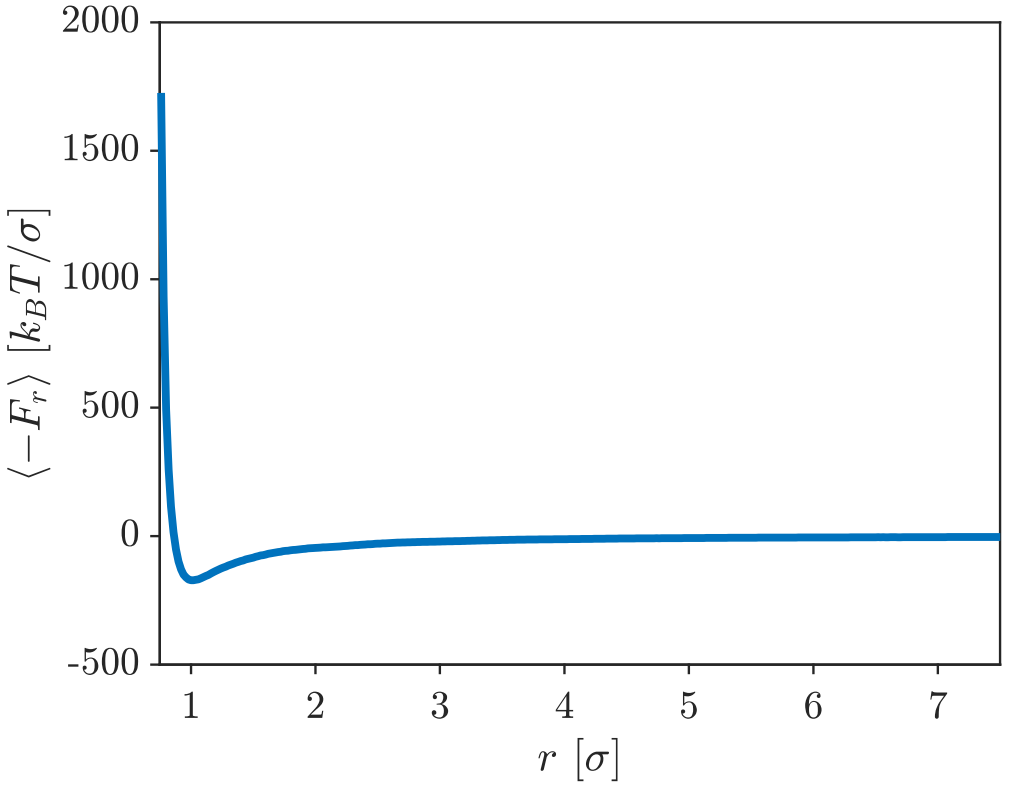
$$U_{ij}^{\mu\mu}(\mathbf{r}) = \frac{1}{4\pi\varepsilon_0}\frac{\boldsymbol{\mu}_i\cdot\boldsymbol{\mu}_j}{|\mathbf{r}_{\mu\mu}|^3} - \frac{3}{4\pi\varepsilon_0}\frac{(\boldsymbol{\mu}_i\cdot\mathbf{r}_{\mu\mu})(\boldsymbol{\mu}_j\cdot\mathbf{r}_{\mu\mu})}{|\mathbf{r}_{\mu\mu}|^5}$$

Potential of Mean Force (PMF) from MD

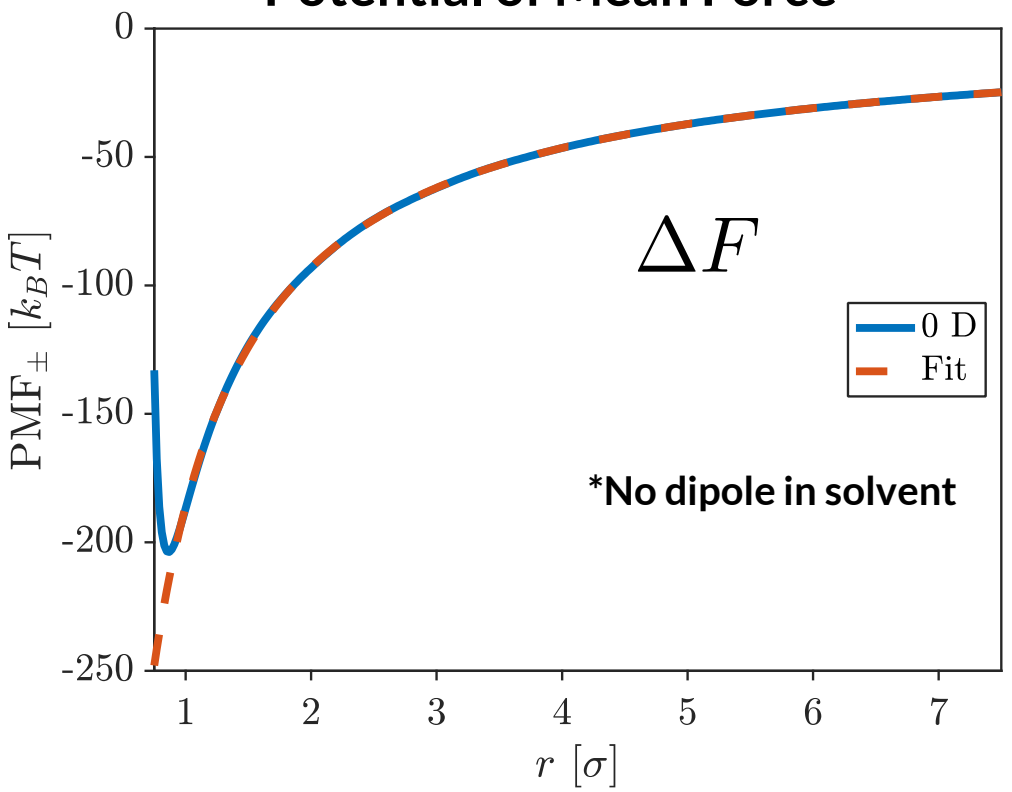
- Appy a force to sample the collective variable



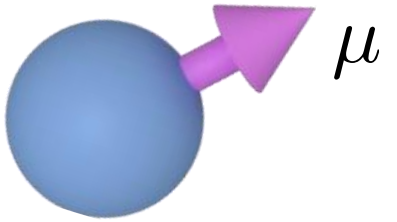
Mean Applied Force along Coordinate

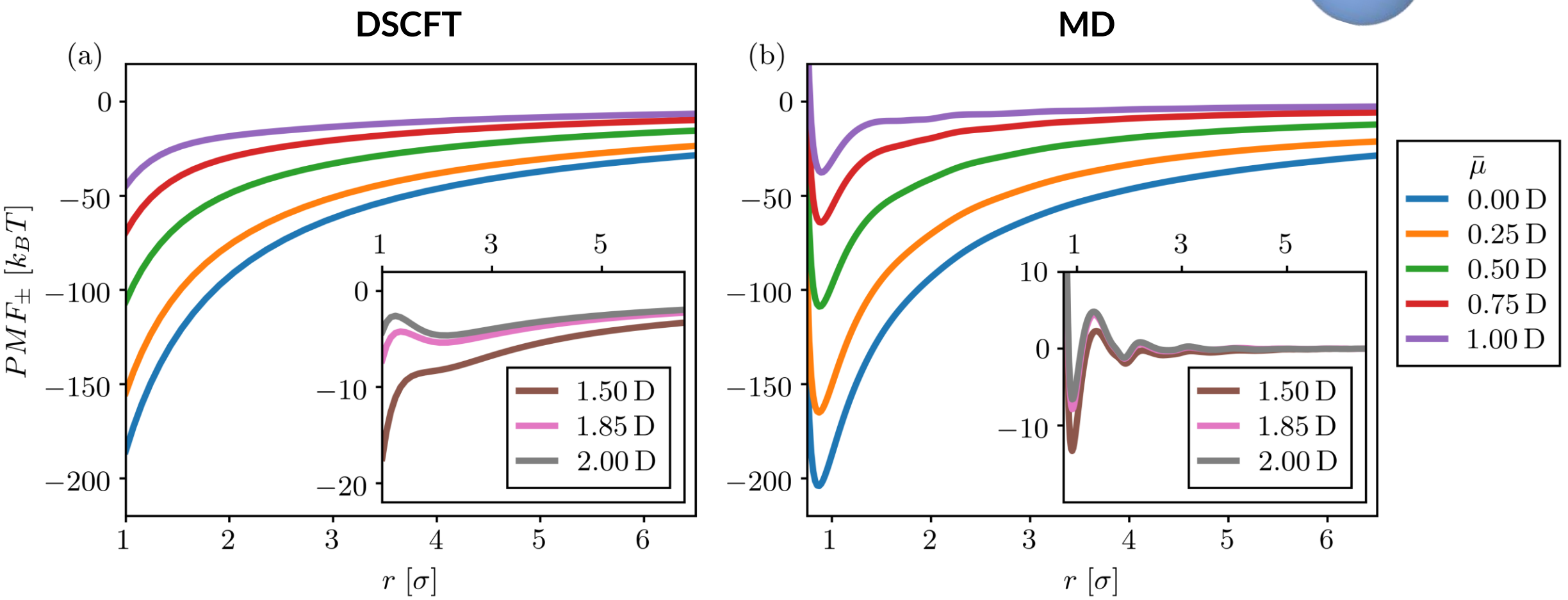


Potential of Mean Force



PMFs from DSCFT and MD simulation



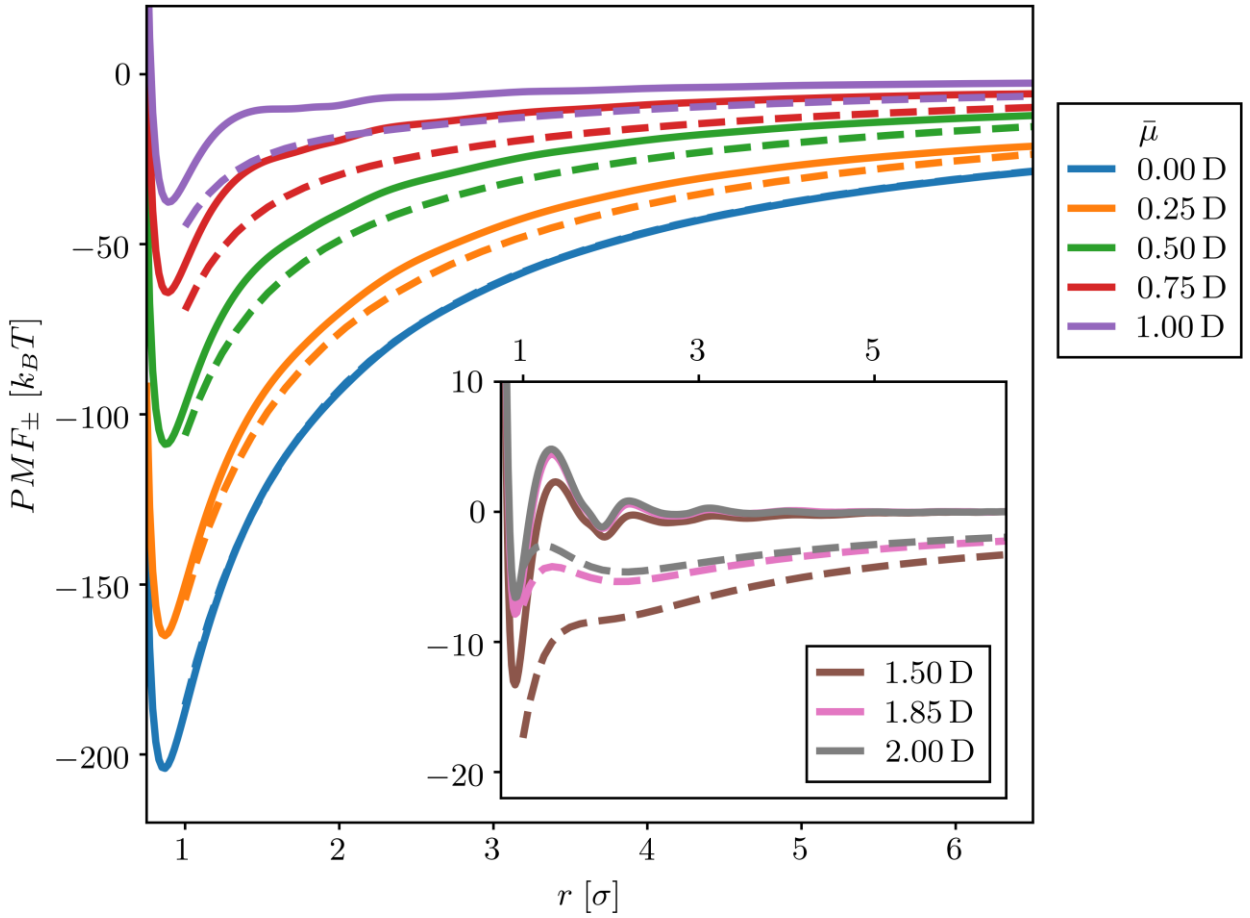


- Increasing dipole moment increases the effective dielectric constant
- PMFs reproduce Coulomb behavior for large ion separation

Comparison of PMFs

- The agreement between methods breaks down at higher dipole moment
  - DSCFT does not account for dipole-dipole correlation

Dipole Moment (D)	ε_r (DSCFT)	ε_r (MD)
0.00	1.00	1.00
0.25	1.21	1.32
0.40	1.54	2.24
0.50	1.84	2.52
0.75	2.89	4.54
1.00	4.37	9.43
1.50	8.57	–
1.85	12.52	–
2.00	14.46	–

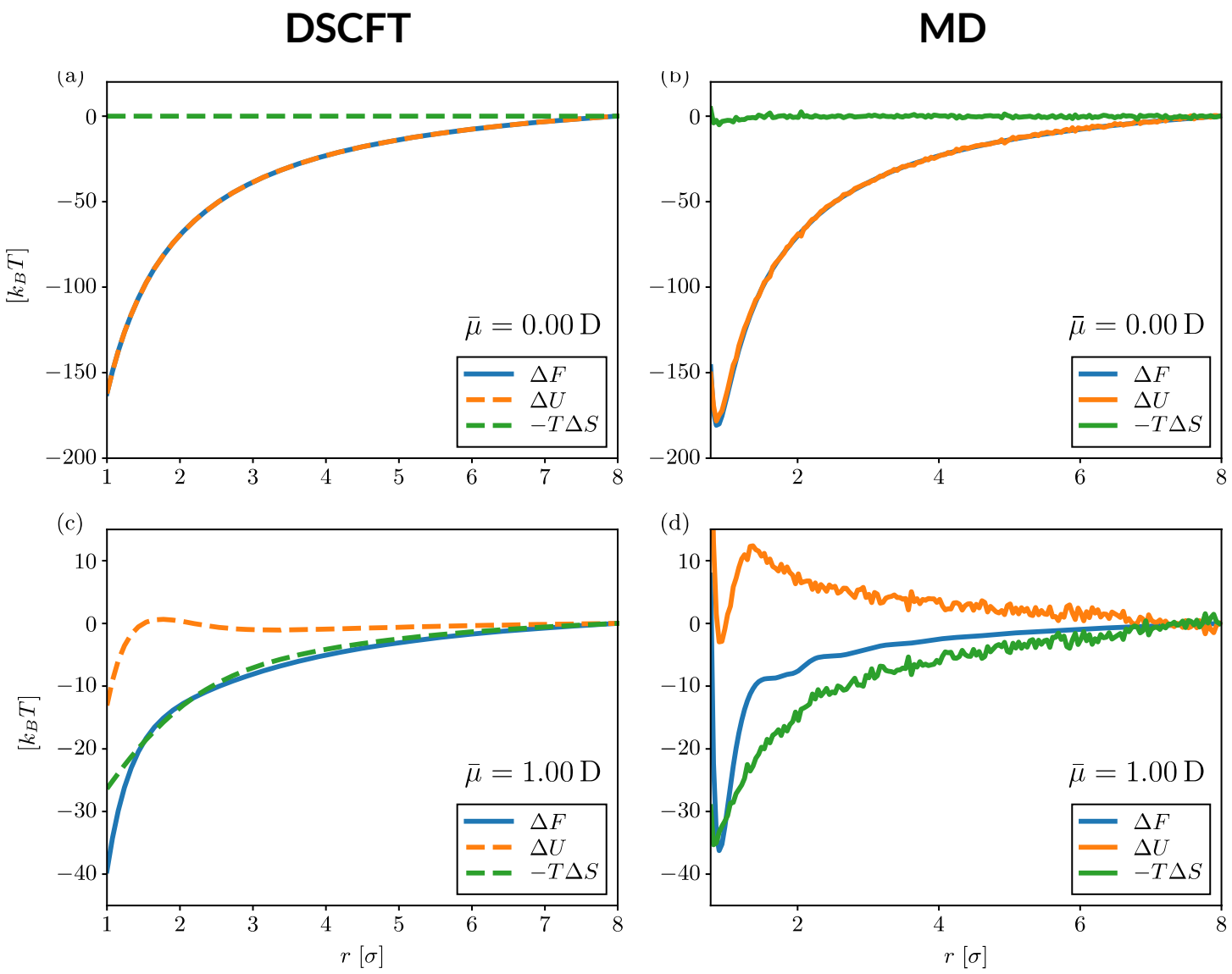


Decomposed free energy $\Delta F = \Delta U - T\Delta S$

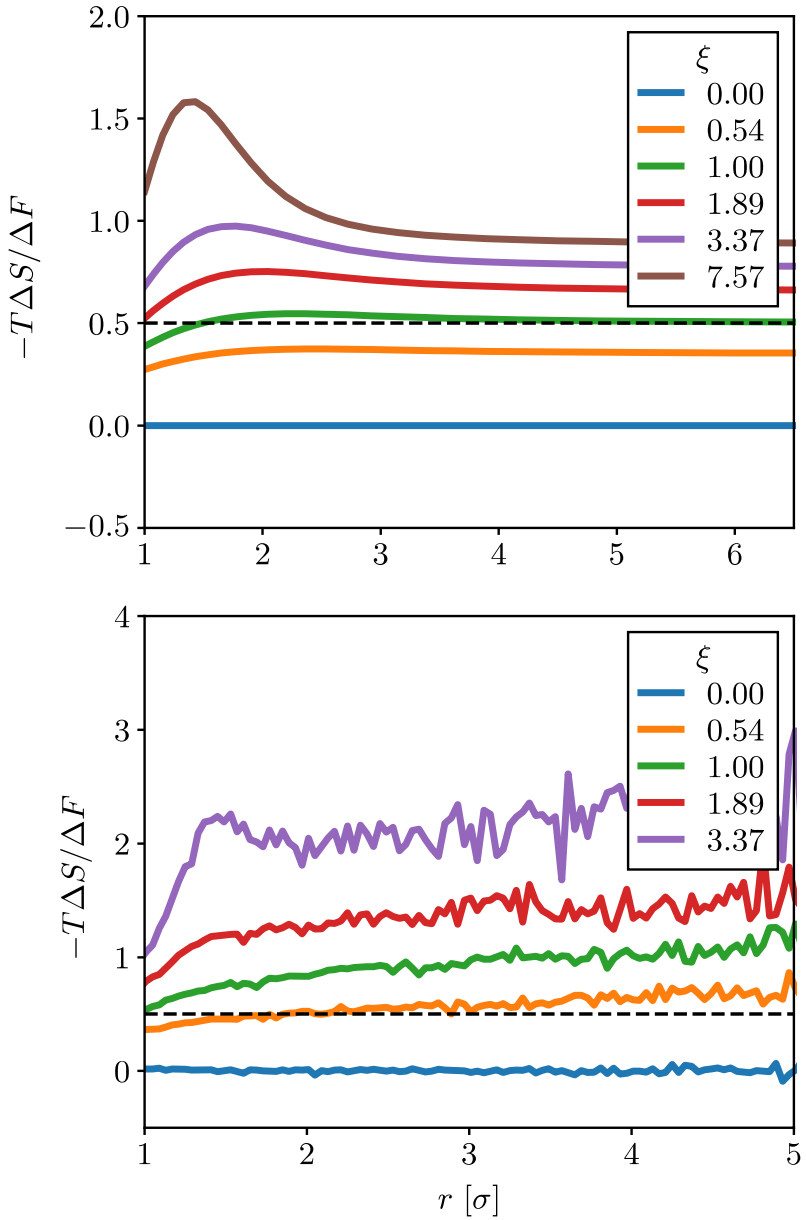
- No dipole case returns Coulomb potential in a vacuum

- For moderate dipole moment, entropy dominates the PMF
- Note the good agreement between DSCFT and MD

for water, $\bar{\mu} = 1.85\,\mathrm{D}$



Ratio of entropy

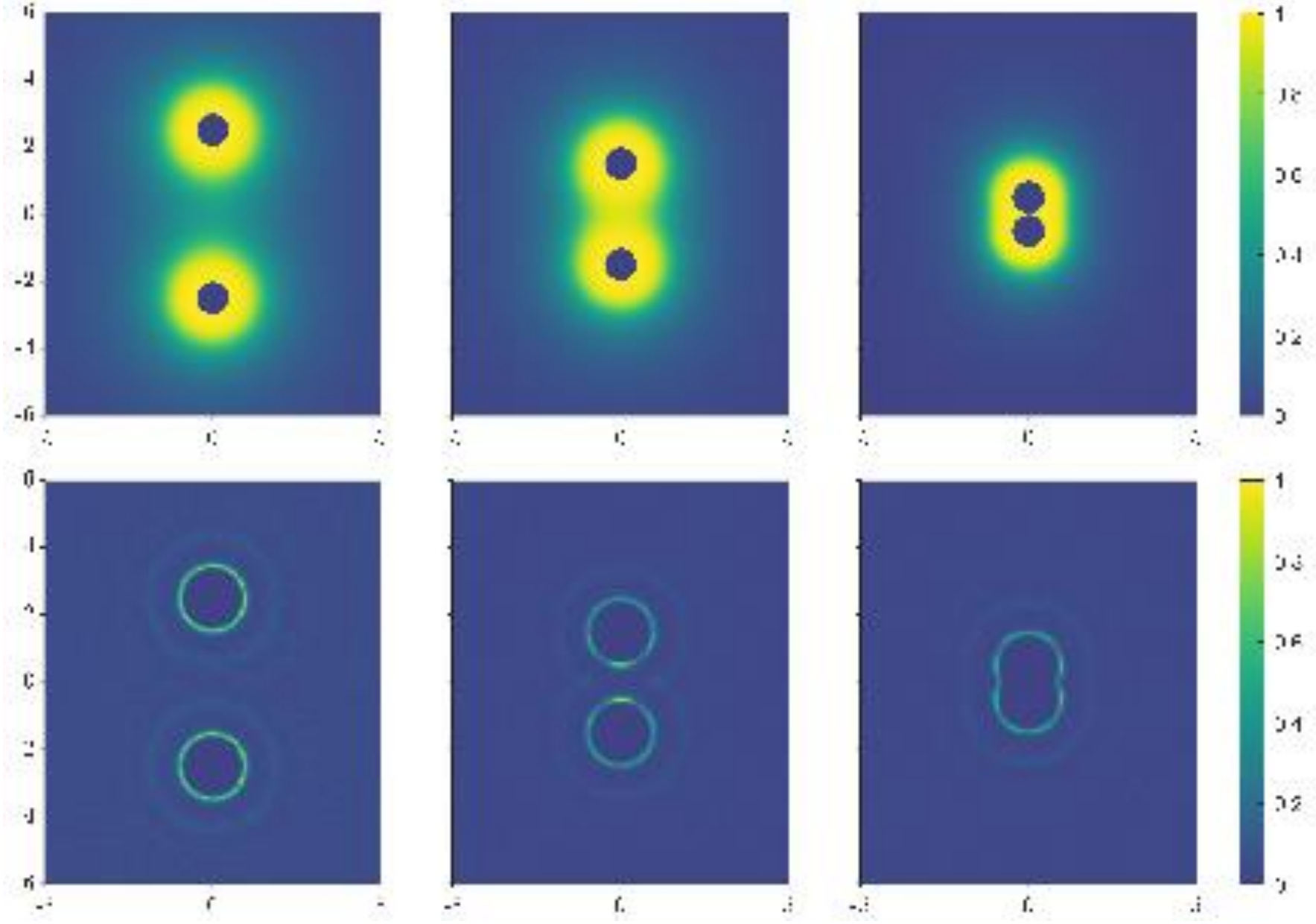


Debye Approximation: $\dfrac{-T\Delta S}{\Delta F} = \dfrac{\xi}{1+\xi}$ $\qquad \xi = \dfrac{\beta\bar{\mu}^2}{3v\varepsilon_0}$

$\xi > 1 \implies$ Entropy dominance!

- Both methods crossover from energy to entropy dominant
- DSCFT recovers the result from Debye in long range
- For large dipole moments, the process is entropic

Visualizing the solvent polarization



DSCFT (Local Orientation)

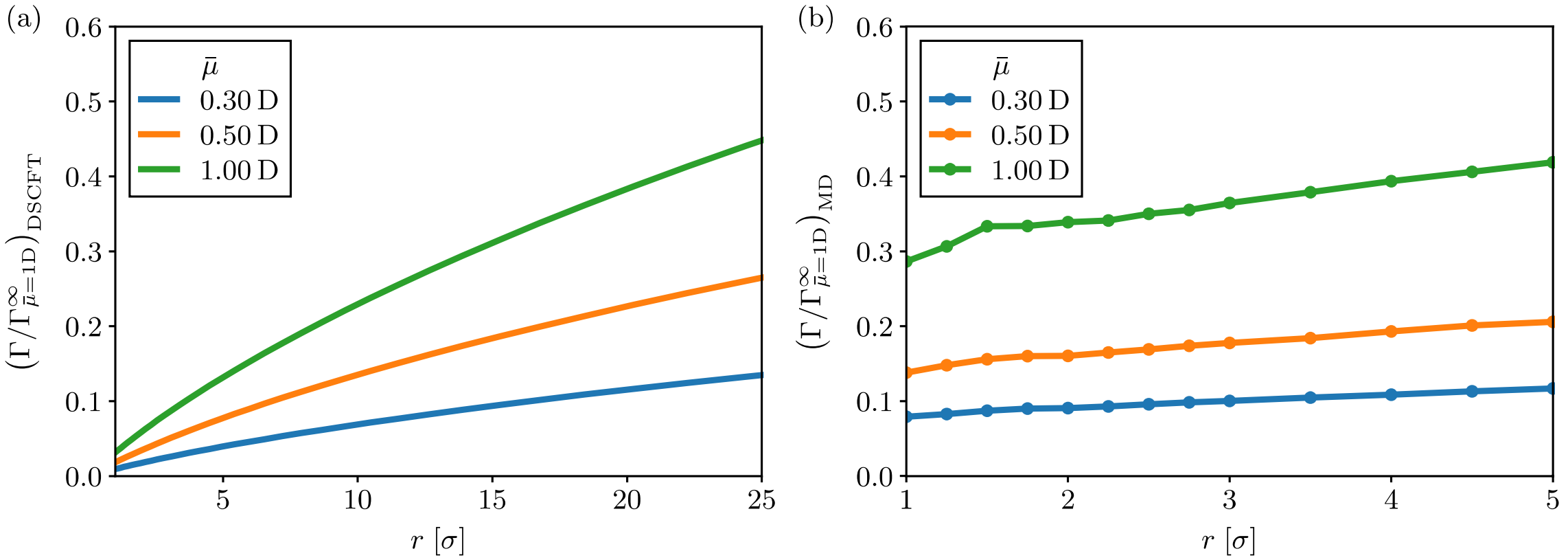
$$|P| = \chi_{\mathrm{or}} |\nabla \phi|$$

MD (Average Dipole)

$$\left|\left\langle \mu(\mathbf{r}) \right\rangle\right|$$

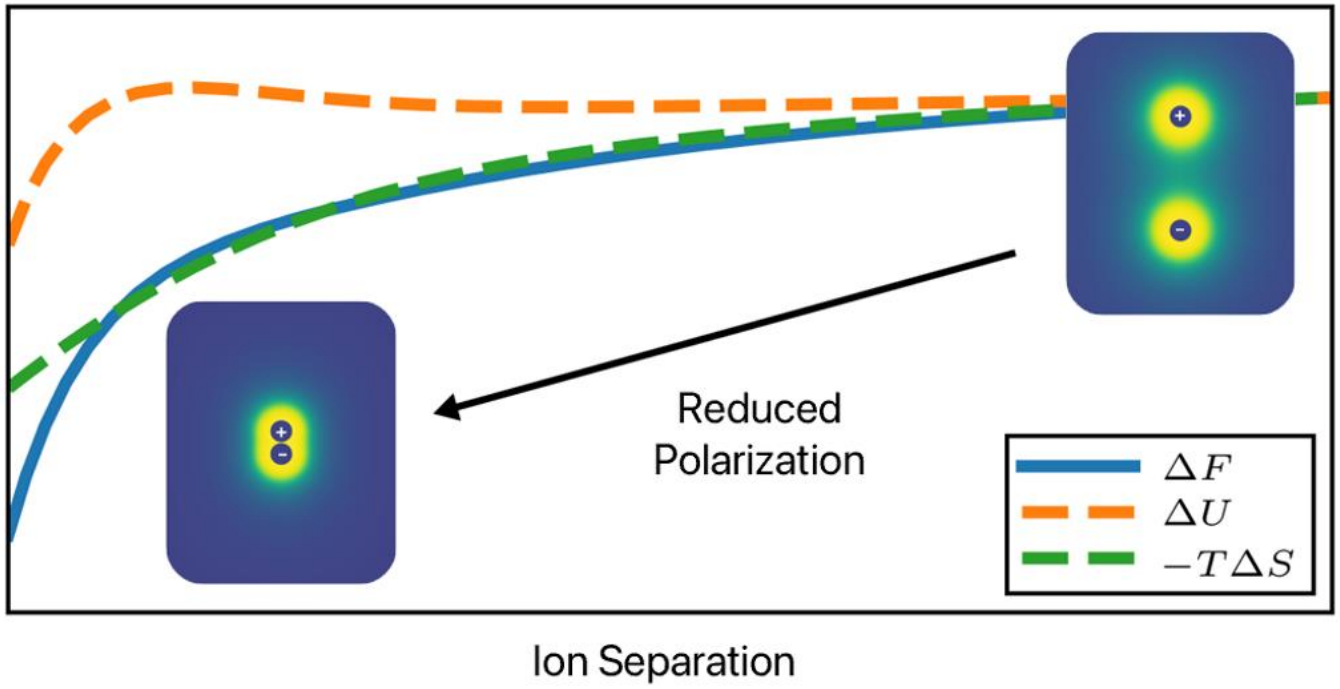
Quantifying the solvent polarization

- The excess polarization decreases as we bring the ions together
- The magnitude of the change increases for increasing dipole strength



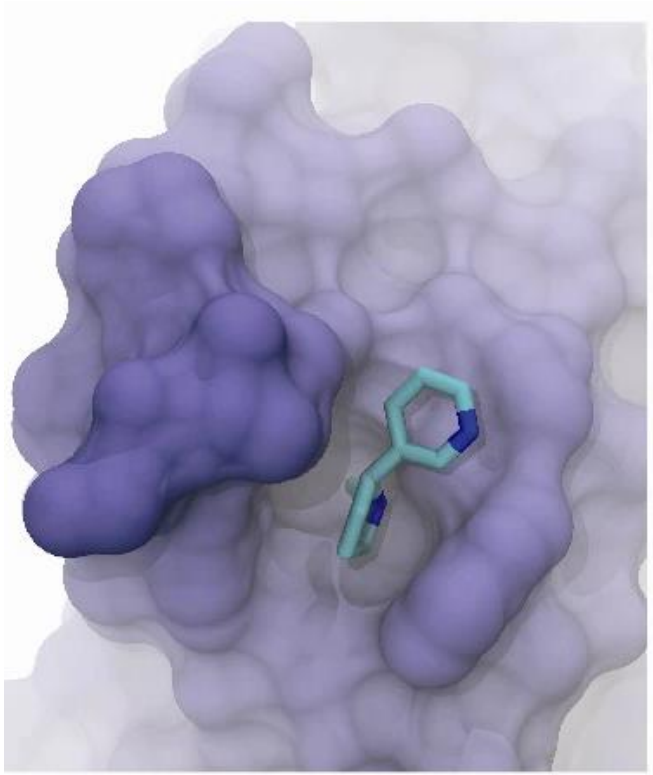
Summary

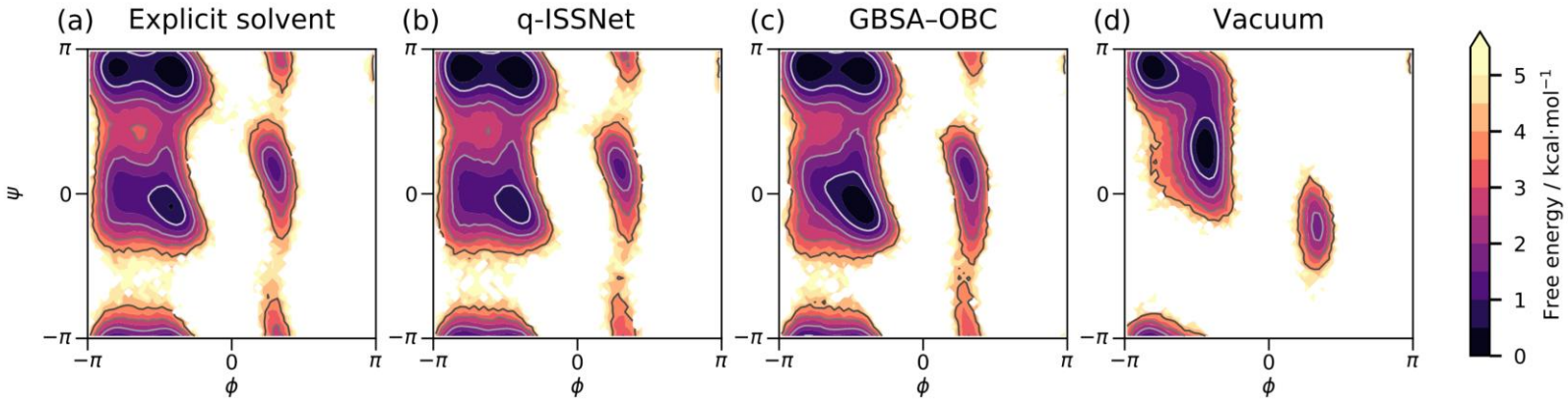
- Implicit solvent models often hide entropy in effective interaction parameters
- If the dipole strength is large enough, the solvent entropy dominates the interaction between two oppositely charged ions



Beyond Two Ions

- Enthalpy-entropy compensation
- Machine-learned implicit solvent models





Chen et al, J. Chem. Phys. 155, 084101 (2021)

Acknowledgements

- Prof. Zhen-Gang Wang
- Sam Varner