How to Distinguish F^- (aq) from Cl^- (aq), Locally ?

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Challenges

Same charge

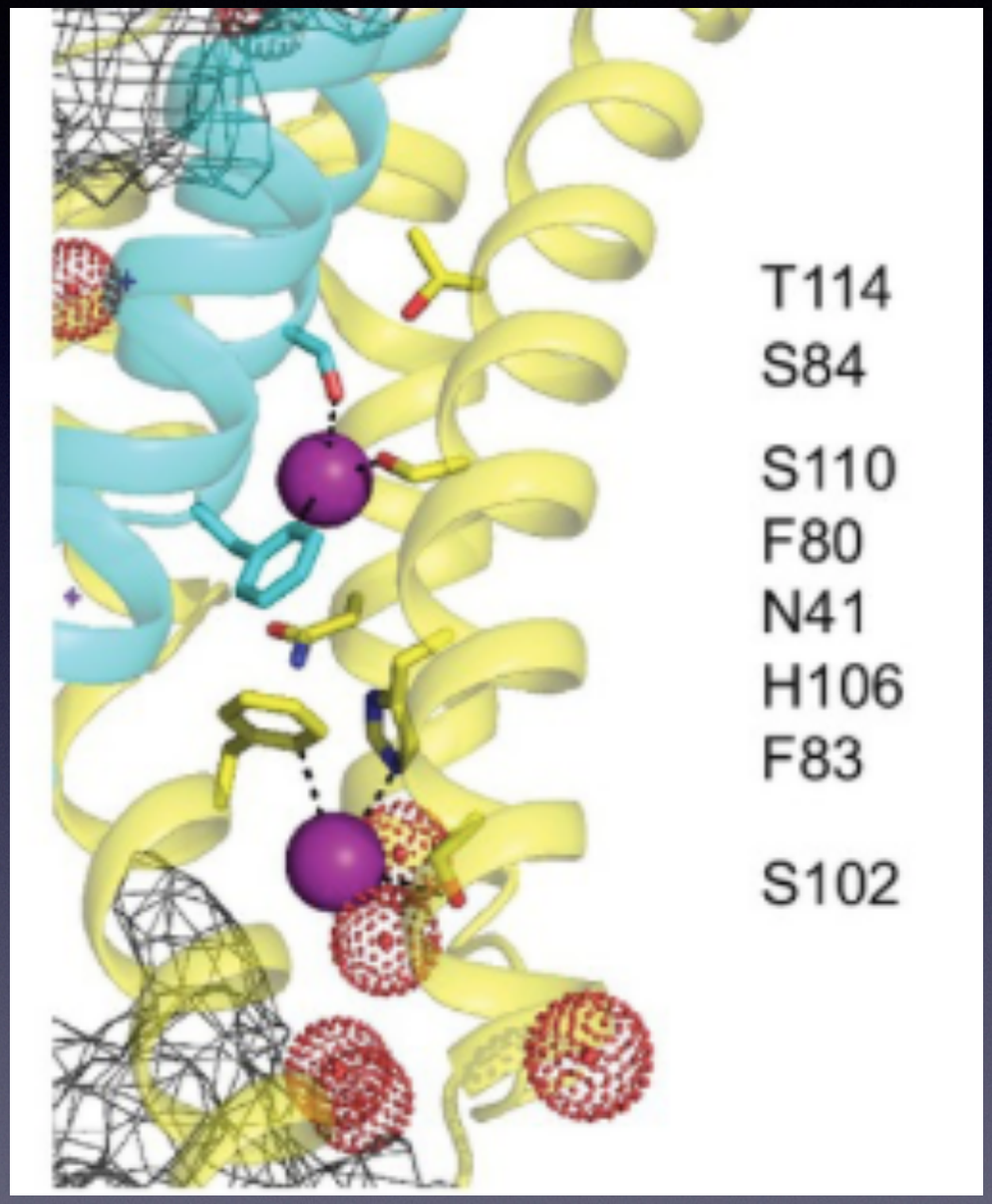
Similar size
(ionic radii)

0.13 nm

0.18 nm

http://abulafia.mt.ic.ac.uk/shannon/ptable.php

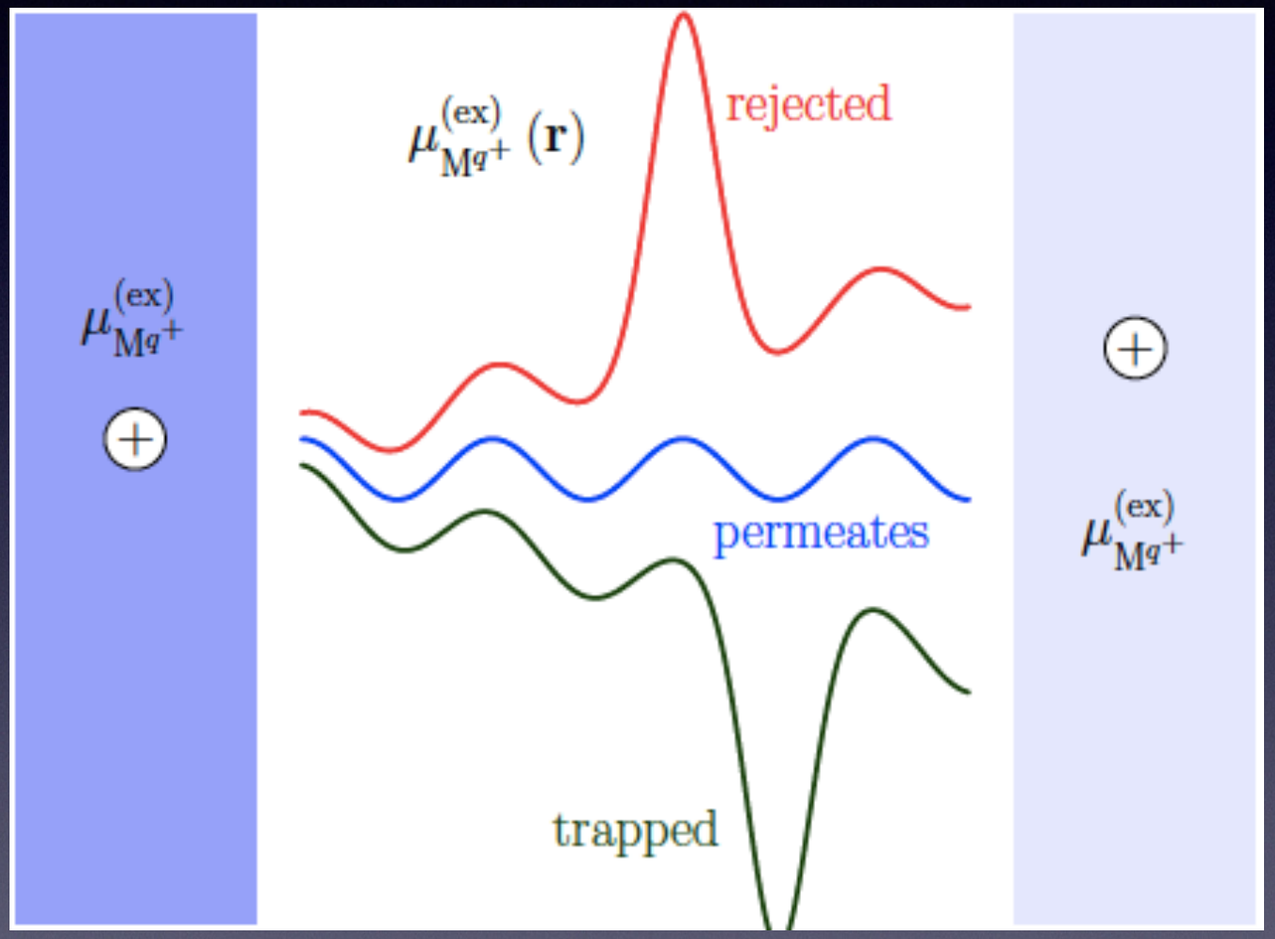
Living example



Fluc channels distinguish F^-/Cl^- — by 10^4!

Miller, et al. *eLife* (2017)

Ion hydration as reference



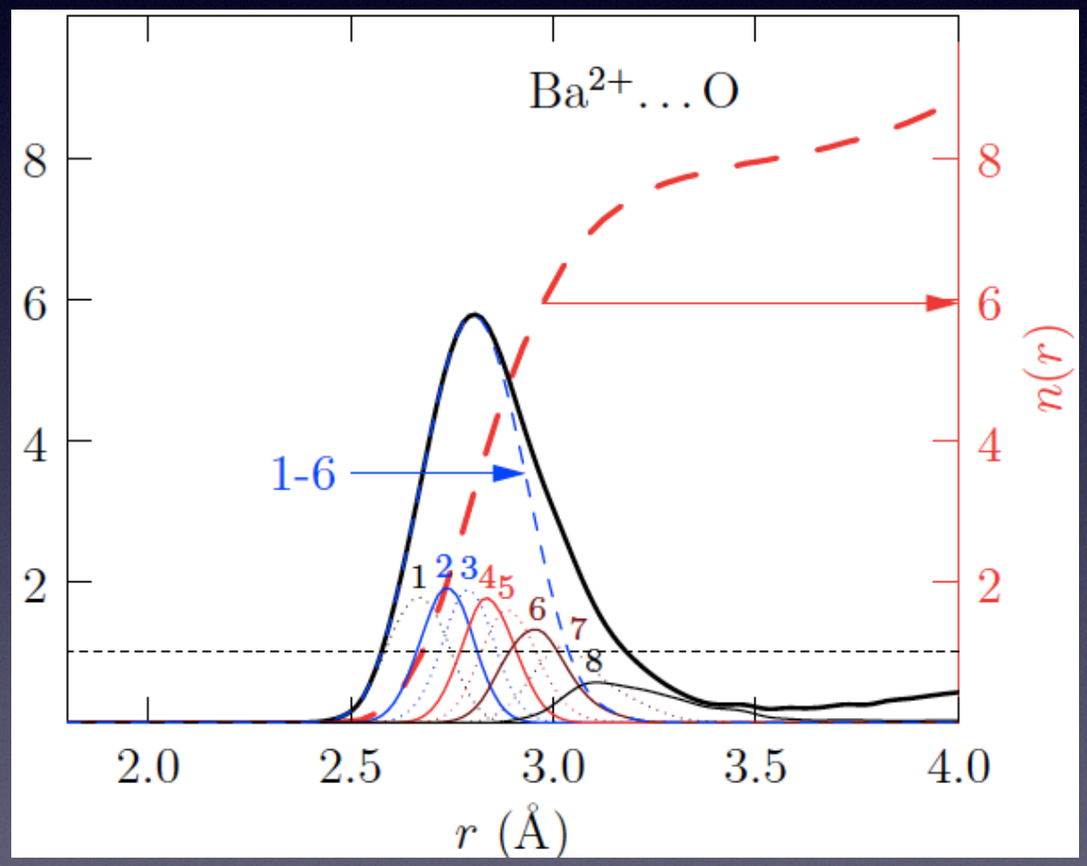
Cl-

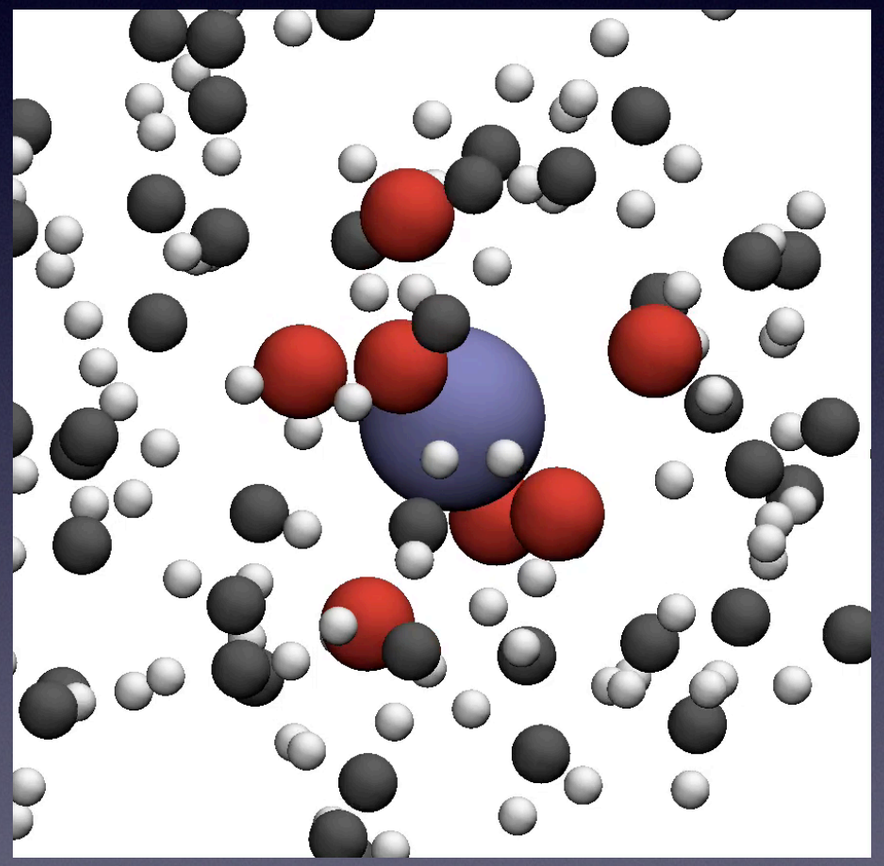
F-

Ion free energy vs channel structure

Chaudhari, SBR, et al. *Acc. Chem. Res.* (in prep)

Measuring local ion hydration structure



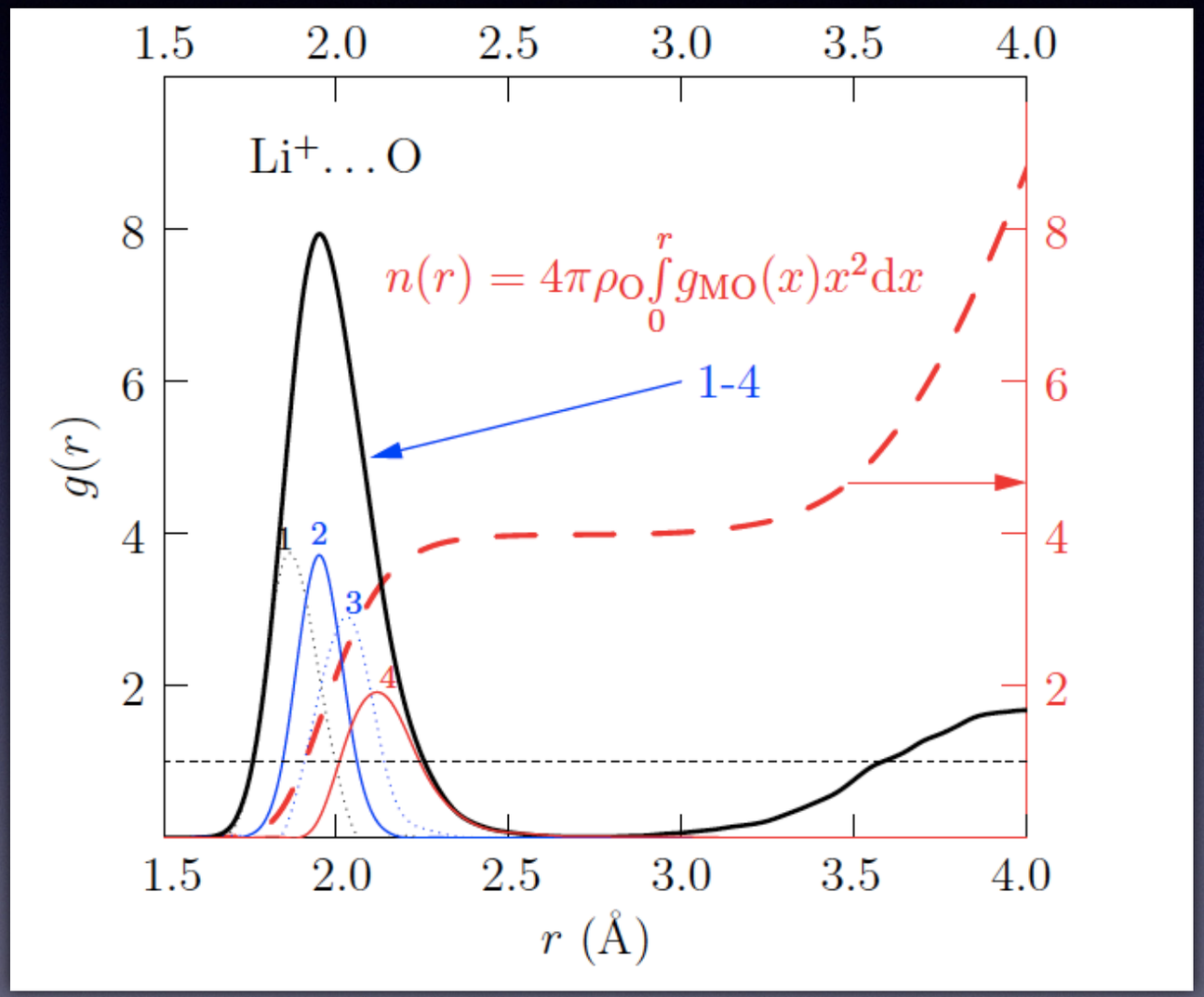


Ab initio molecular dynamics (AIMD)

Chaudhari, Soniat, SBR *JPCB* (2015)

Chaudhari, SBR *JCP* (2018)

Experiments agree with simulations!



4 vs 6 motivates new experiments

SBR, et al. *JACS* (2000)

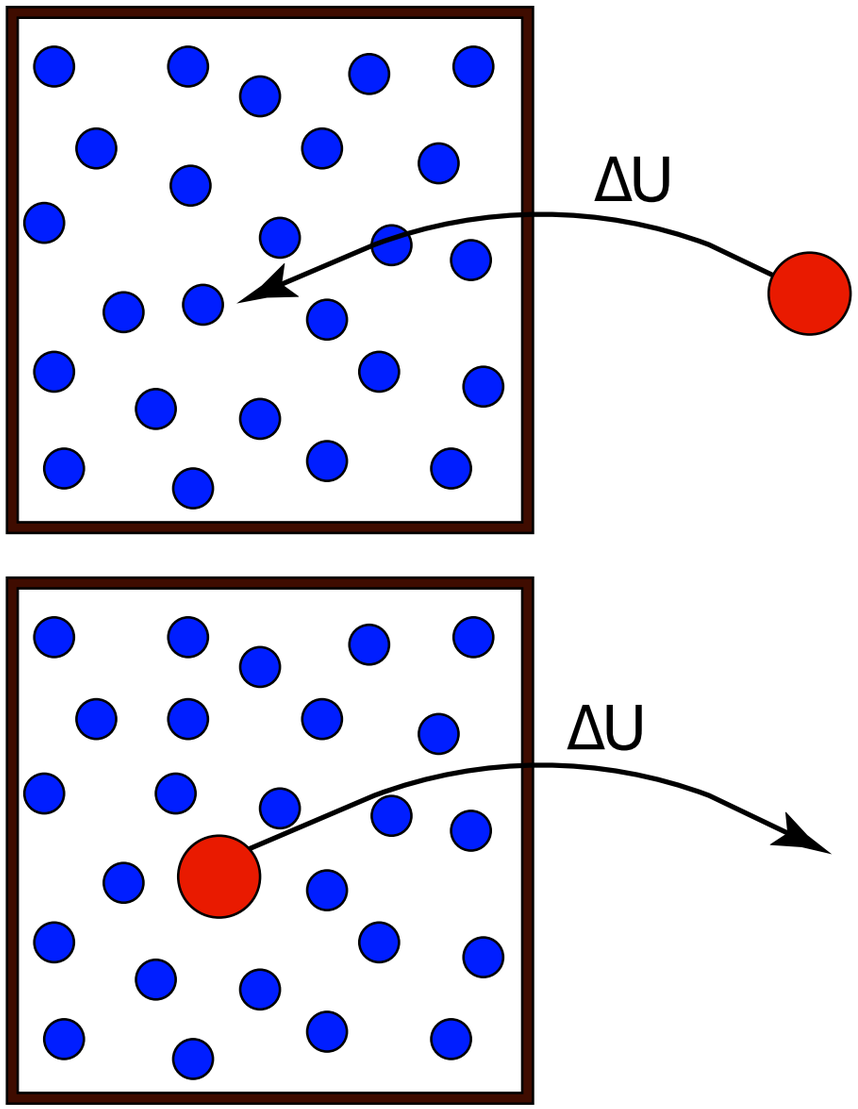
Neilson, SBR, et al. *JPCB* (2015)

Comparison (peak position)

Ion^{+}	AIMD	EXP	Ion^{2+}	AIMD	EXP
Li	1.95 [53,133]	1.96 [44]	Mg	2.09 [56]	2.04 [146]
Na	2.37 [26]	2.38 [47]	Ca	2.45 [56]	2.43 [146,147]
K	2.73 [26,28]	2.73 [48]	Sr	2.64 [30]	2.63 [148,149]
Rb	2.95 [43]	3.10 [150]	Ba	2.81 [55]	2.80 [144]

Chaudhari, Vanegas, Muralidharan, Pratt, SBR, *Acc. Chem. Res.* (in prep)

Computing free energy



Hydration

Forward Widom:

$$e^{-\beta\mu^{(ex)}} = \left\langle\left\langle e^{-\beta\Delta U}\right\rangle\right\rangle_0$$

$\langle\langle..\rangle\rangle_0$: uncoupled averaging

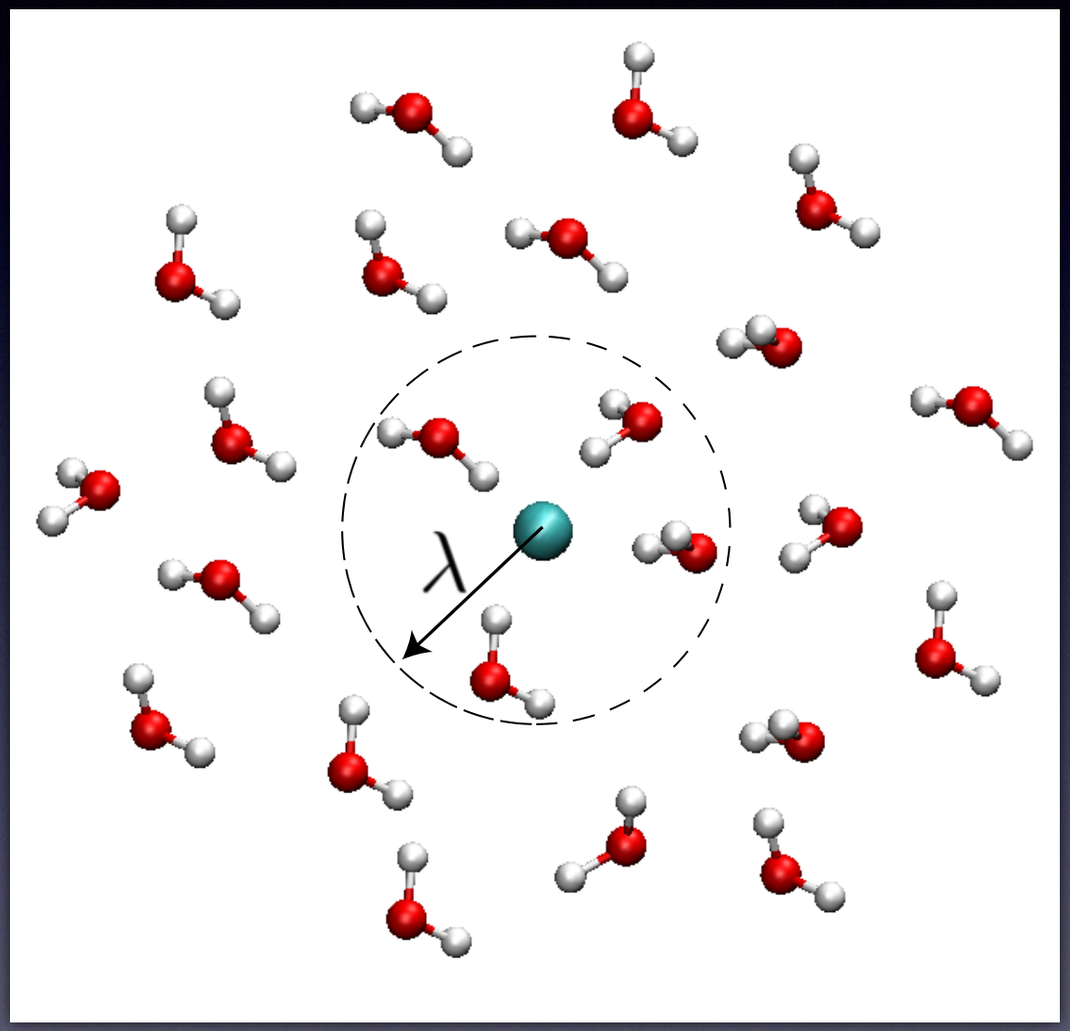
Reverse Widom:

$$e^{+\beta\mu^{(ex)}} = \left\langle e^{+\beta\Delta U}\right\rangle$$

Excess chemical potential

Beck, Paulaitis, Pratt The Potential Distribution Theorem … (2016)

Computing free energy - QCT



$$\chi_n = \begin{cases} 1, & \text{if occupied by n ligands} \\ 0, & \text{otherwise} \end{cases}$$

$$p(n) = \langle \chi_n \rangle = \frac{\left\langle \left\langle e^{-\beta \Delta U} \chi_n \right\rangle \right\rangle_0}{\left\langle \left\langle e^{-\beta \Delta U} \right\rangle \right\rangle_0}$$

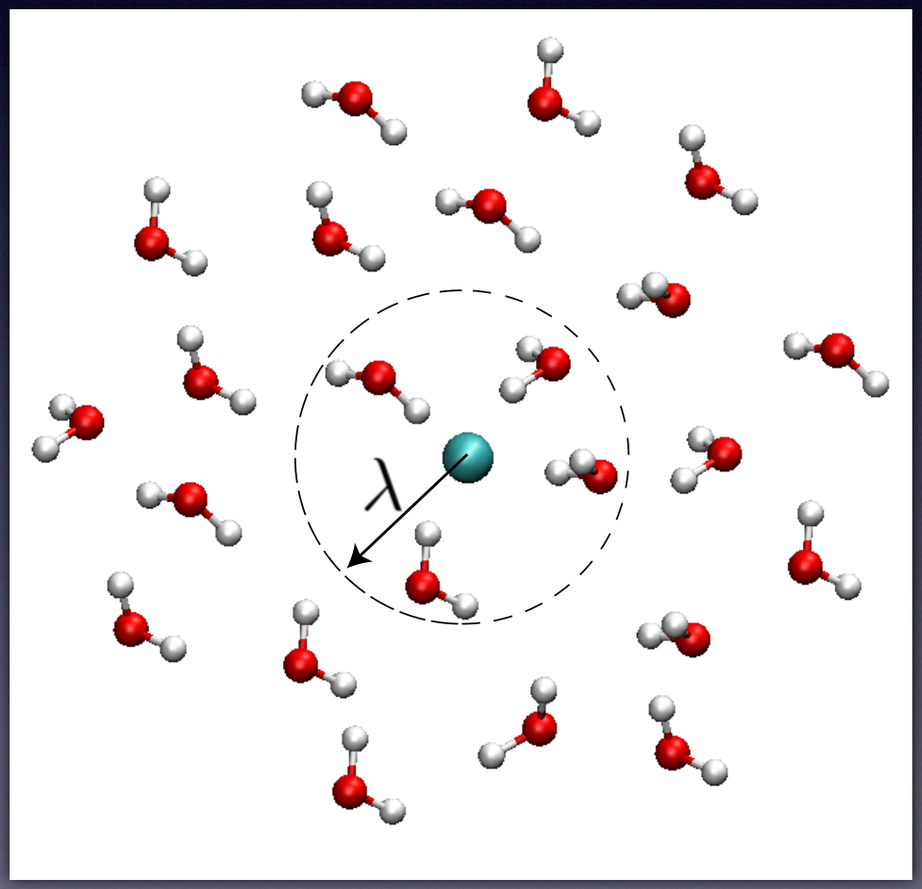
$$p(n) = \frac{\left\langle \left\langle e^{-\beta \Delta U} | n \right\rangle \right\rangle_0 p^{(0)}(n)}{e^{-\beta \mu^{(ex)}}}$$

Quasi-chemical theory (QCT)
(direct or cluster)

Pratt, SBR *"Red Book"*(1999) Rogers, SBR, et al *Ann Rep Comp Chem* (2013)

Cluster-QCT free energy

$$\beta\mu^{(\mathrm{ex})}_{\mathrm{F}^-} = -\ln K_n^{(0)}\rho^n + \ln p(n) + \left\{\beta\mu^{(\mathrm{ex})}_{\mathrm{F(H_2O)}_n^-} - n\beta\mu^{(\mathrm{ex})}_{\mathrm{H_2O}}\right\}$$



$$\mathrm{F}^- + n\mathrm{H_2O} \overset{K_n}{\rightleftharpoons} \mathrm{F(H_2O)}_n^-$$

$$(p(0)\rho^n) \times K_n = p(n)$$

Define $K_n^{(0)}$: Equilibrium constant with reactants and products treated as ideal gases.

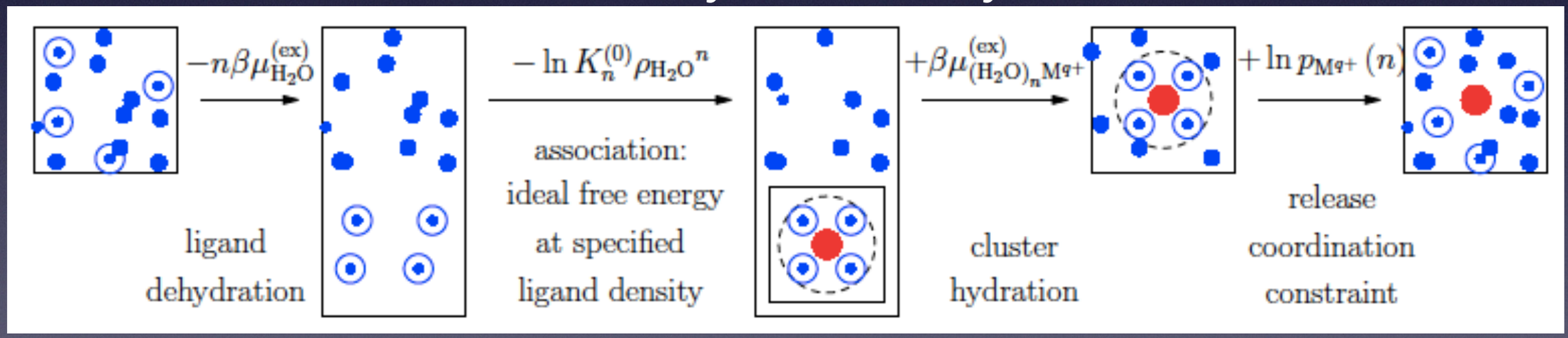
Exact for any n, λ

Permits QM/AIMD for $K_n^{(0)}$, $p(n)$

Cluster QCT free energy

$$\beta\mu_{F^-}^{(ex)} = -\ln K_n^{(0)} \rho^n + \ln p(n) + \left\{ \beta\mu_{F(H_2O)_n^-}^{(ex)} - n\beta\mu_{H_2O}^{(ex)} \right\}$$

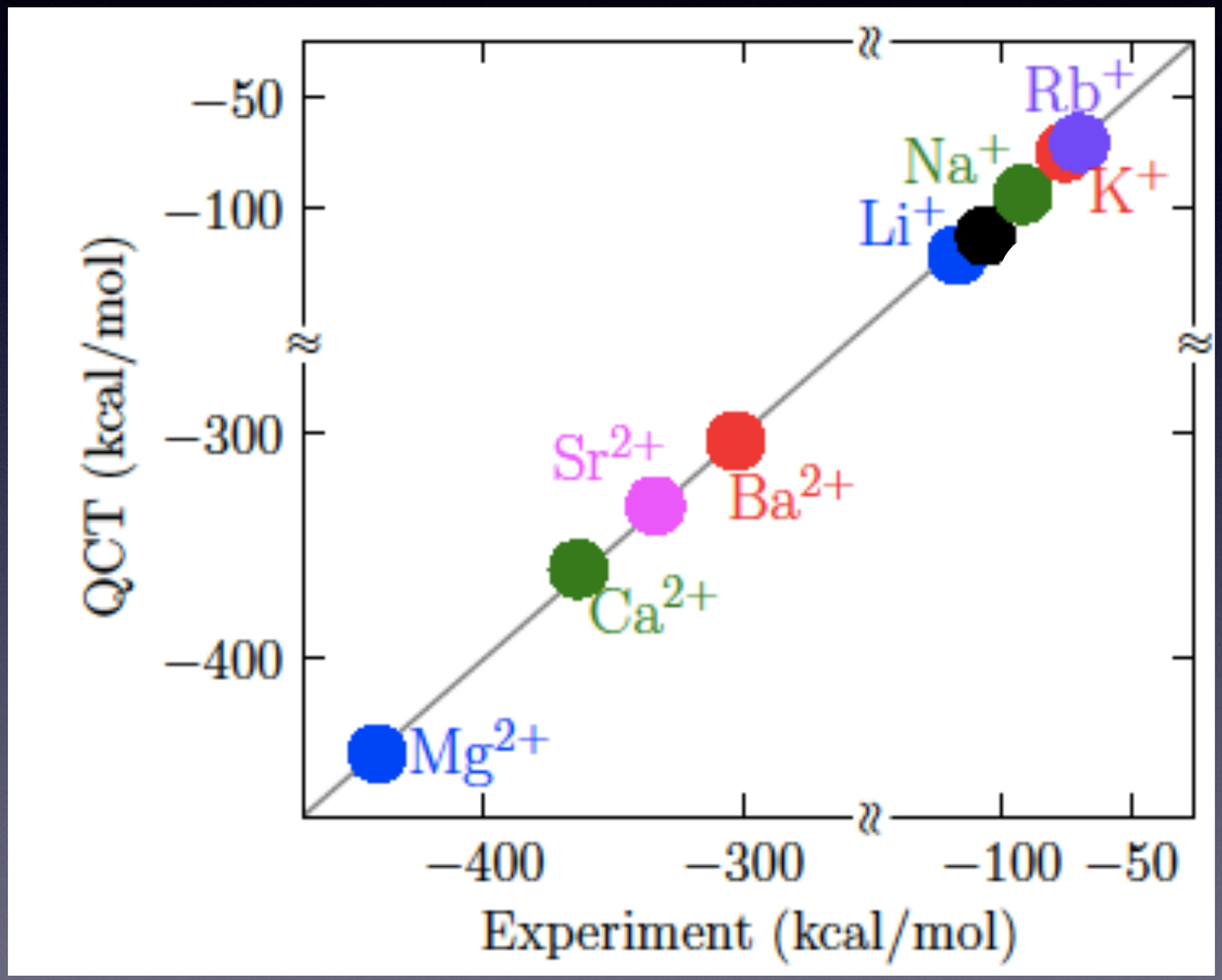
Thermodynamic Cycle



Harmonic cluster vibrations typically assumed

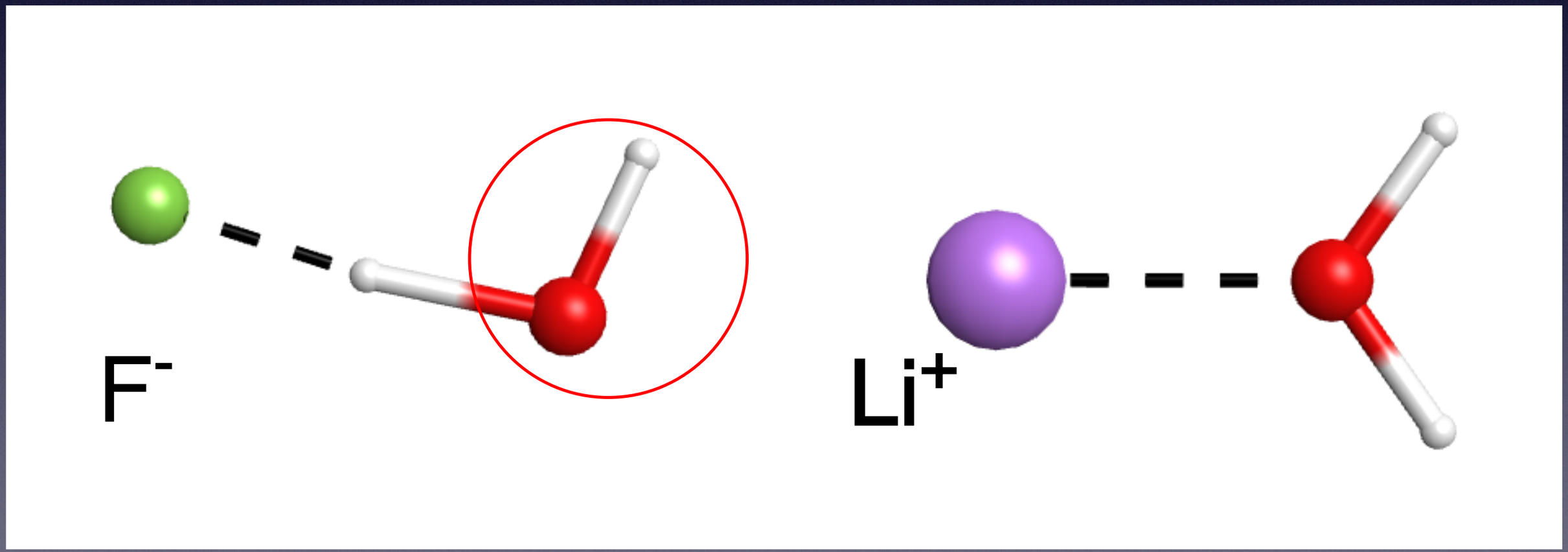
Single structures typically analyzed in cluster hydration

QCT free energies

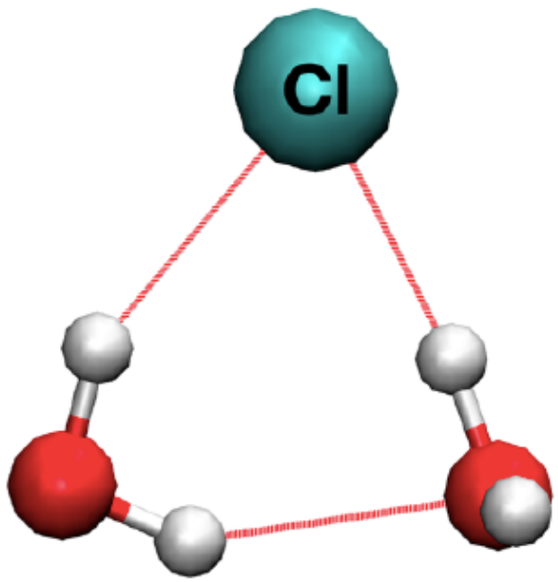


Cation hydration agrees with experiment

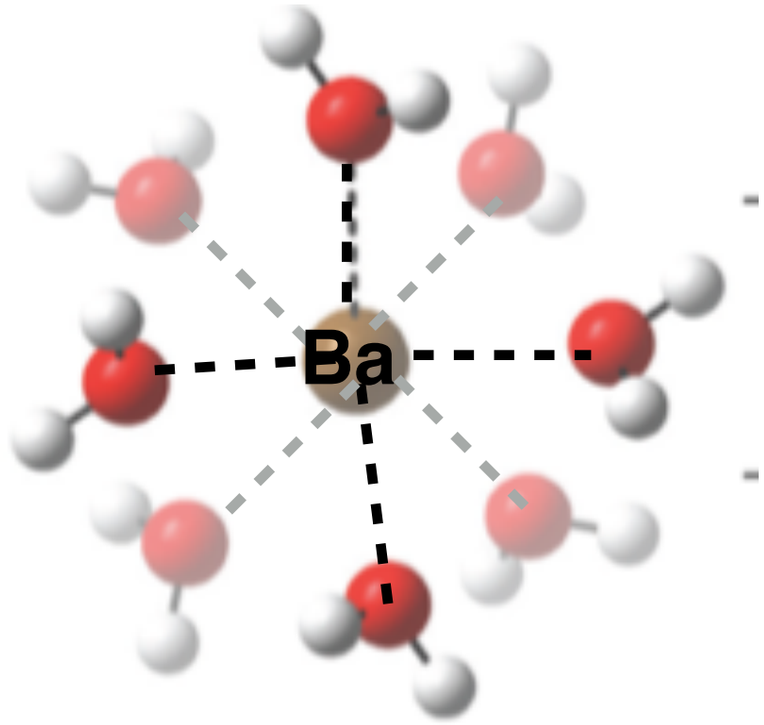
i. Anions interact differently than cations (anion-H)



ii. Anions interact differently than cations (water-water vibrations)

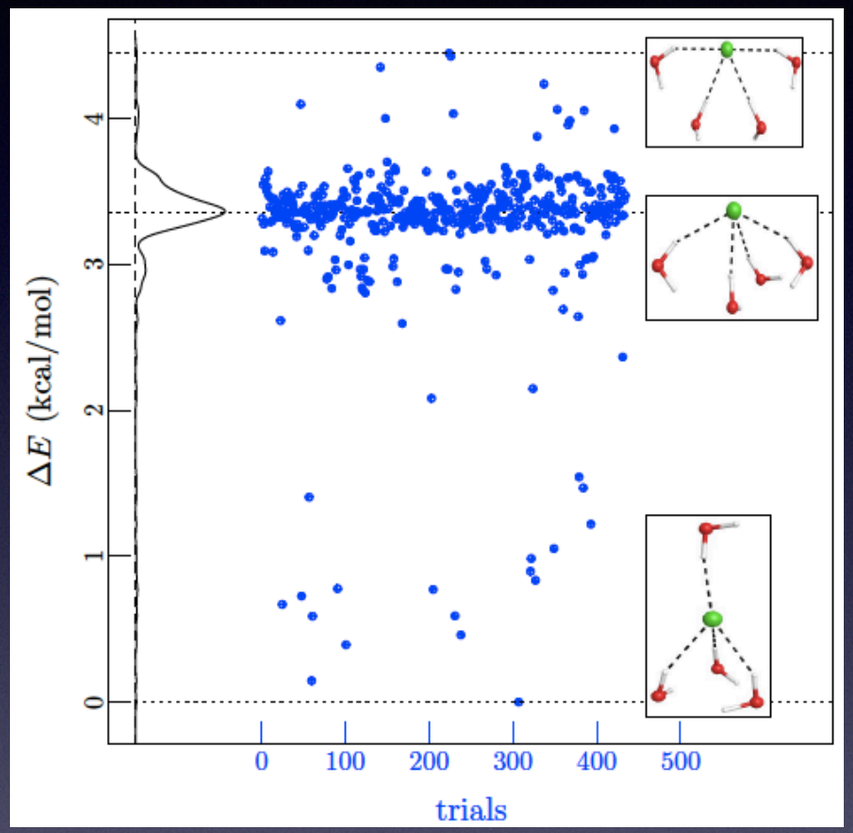


anharmonic vibrations

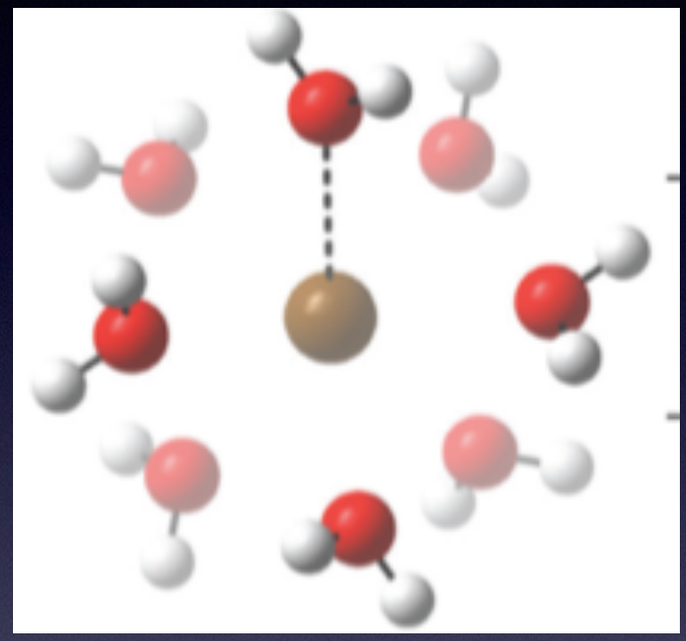


harmonic vibrations

iii. Anions interact differently than cations (competing structures)



many low energy structures (Cl^-)
(sampled from AIMD & optimized in gas)

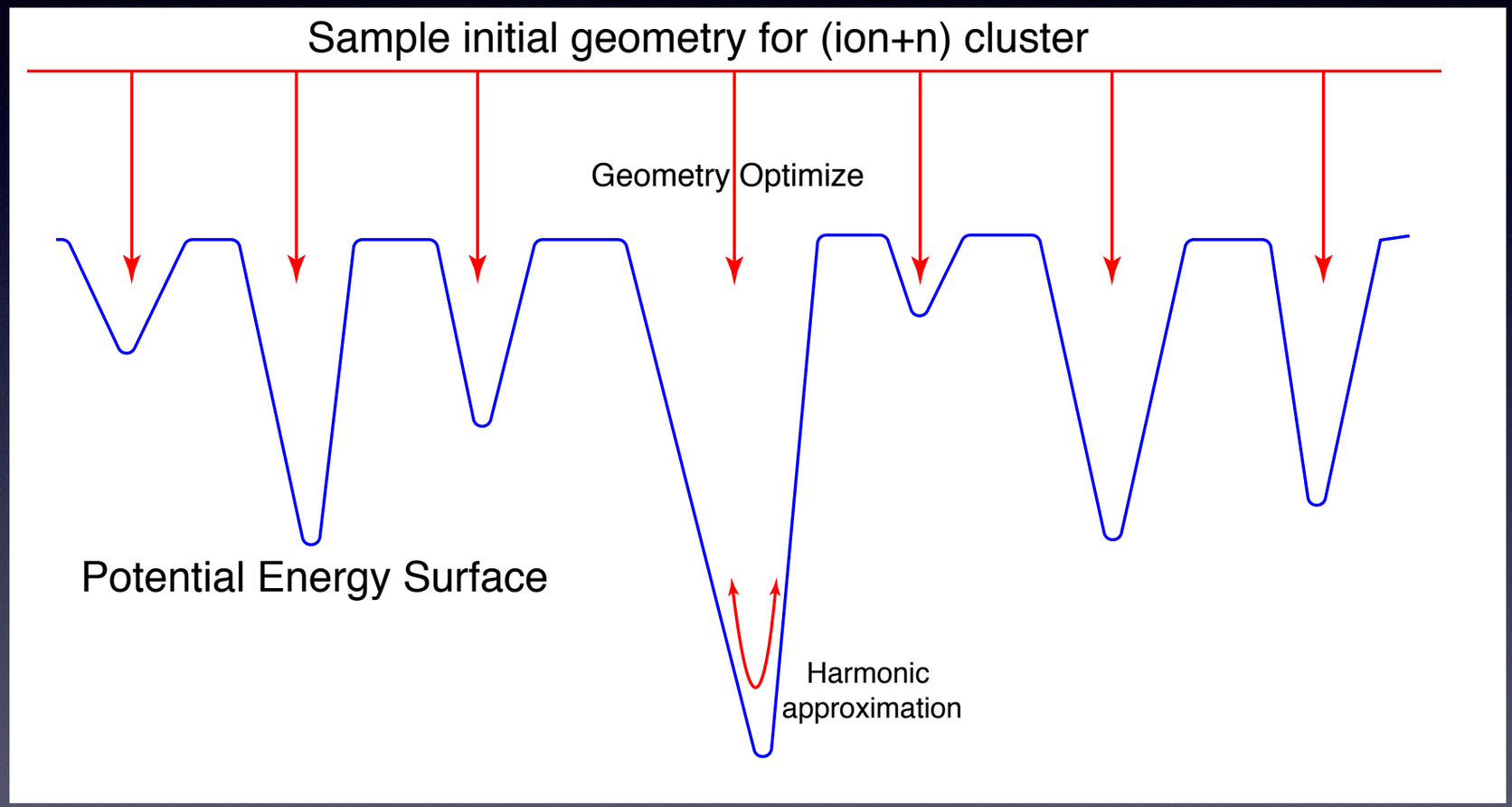


one low energy structure (Ba^{2+})

Need:

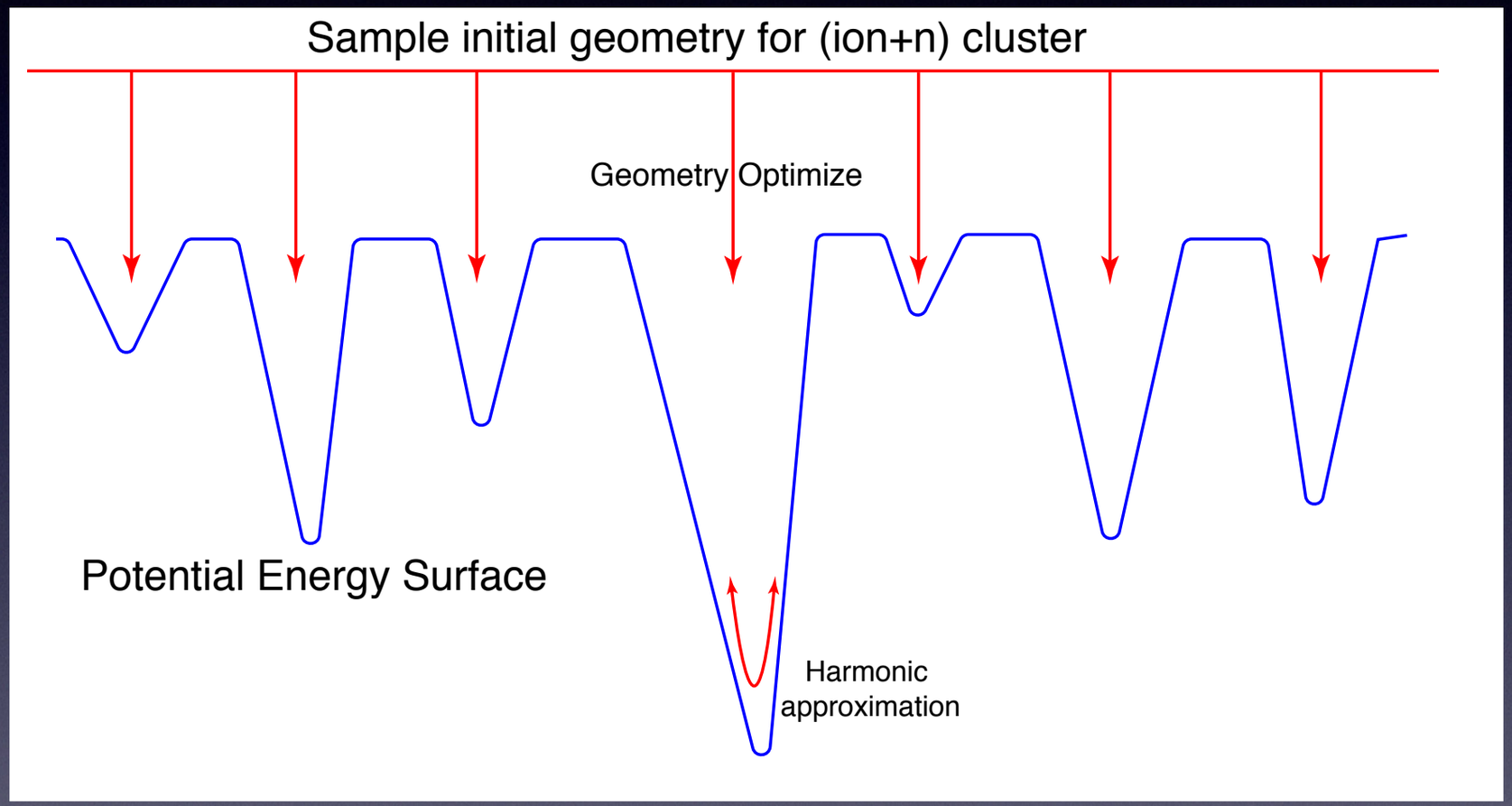
- lowest E structure for $K^{(0)}$
- liquid distribution of structures for $\mu^{(ex)}_{F(H_2O)_n}$

Challenges of computing anion hydration



Ion-H interactions
Competing structures
Anharmonic water-water vibrations

New approach to anion hydration



Ion-H interactions — analyze (structure)
Competing structures — treat (Widom)
Anharmonic vibrational motions — dynamics (ADMP)

Results $F^-(aq)$ & $Cl^-(aq)$

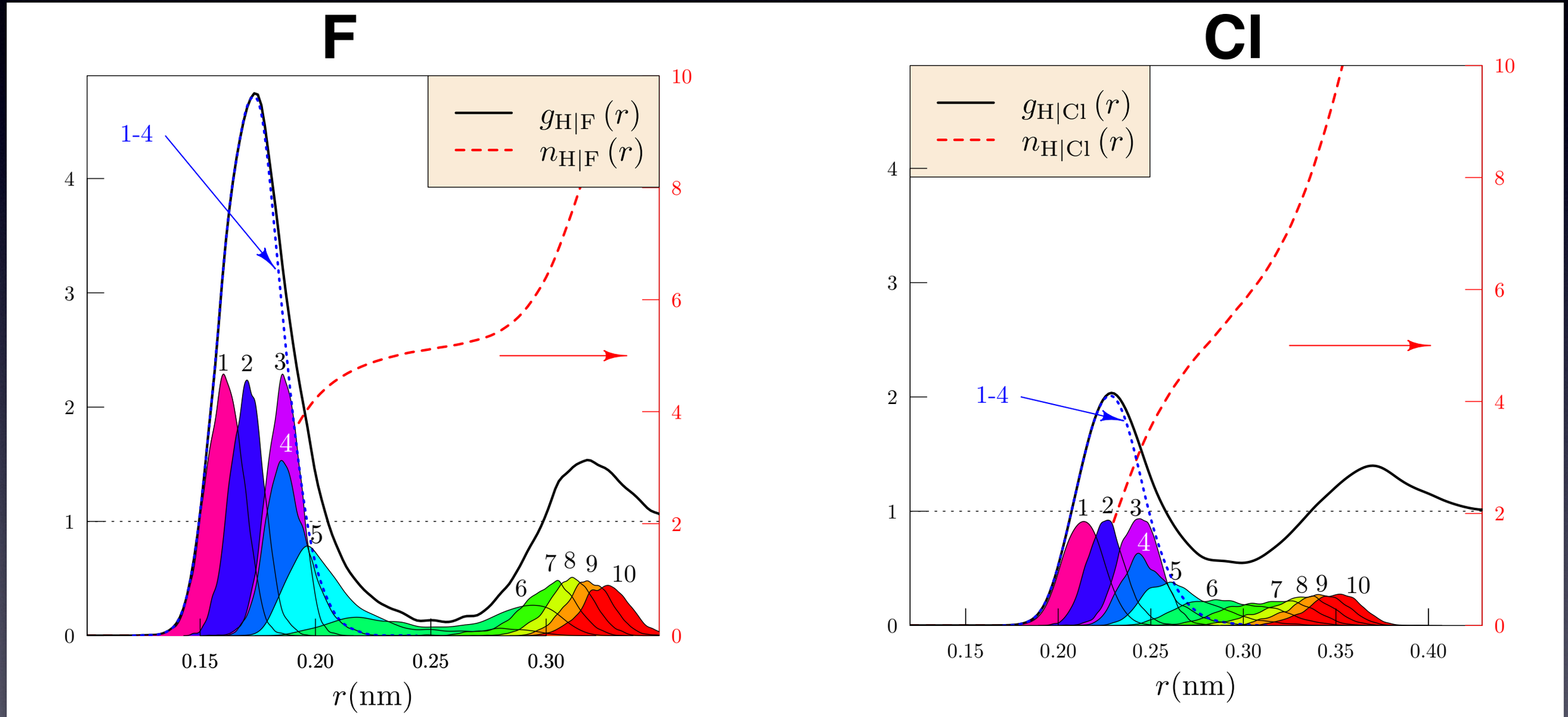
Muralidharan, Chaudhari, Pratt, Rempe, *Chem. Phys. Lett.: X (Frontiers)* (2019).
Muralidharan, Pratt, Chaudhari, Rempe, *J. Phys. Chem. A* (2018).
Chaudhari, Rempe, Pratt, *J. Chem. Phys.* 147:161728 (2017).

Cl & F
F
F

Sabo, Jiao, Varma, Pratt, SBR *Ann. Rep. Prog. Chem.: Sect. C* 109:266 (2013).
Sabo, Varma, Martin, SBR *J. Phys. Chem. B* 112:867 (2008).

Rb
H_2

Radial distribution function g(r): X- to H



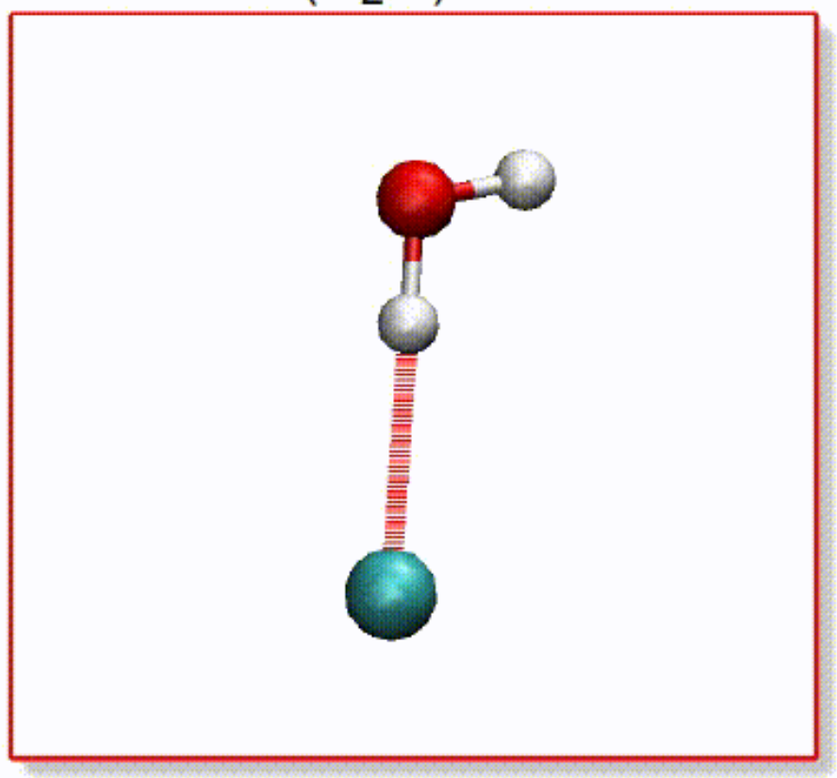
F & Cl same **local** coordination (4 waters)

F ligands **tighter**

Different dynamics (gas) — dipole vs OH-F

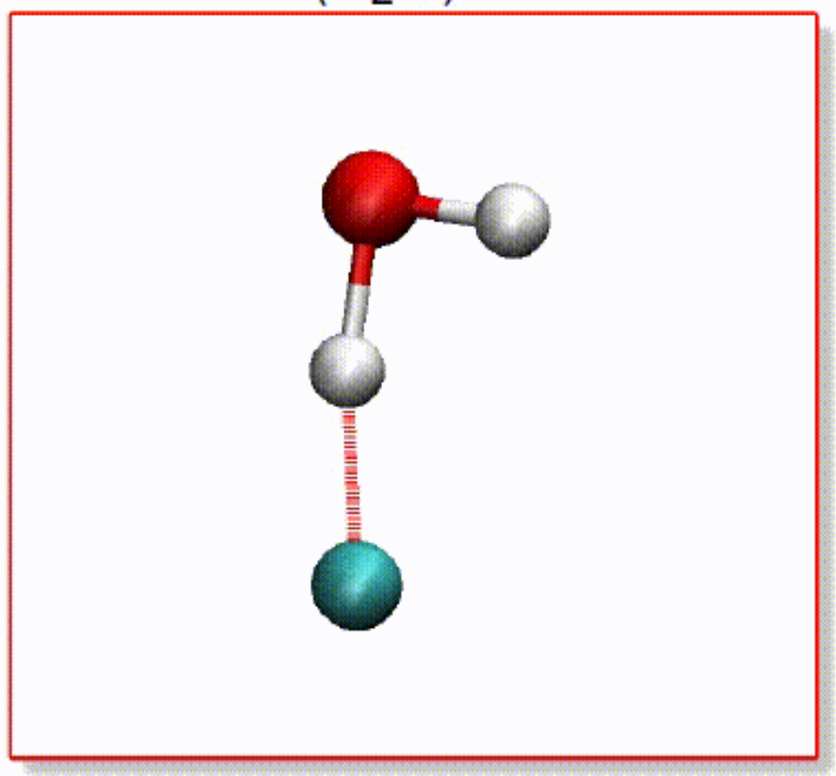
Cluster dynamics using ADMP (5 ps, 300K)

$(H_2O)Cl^-$



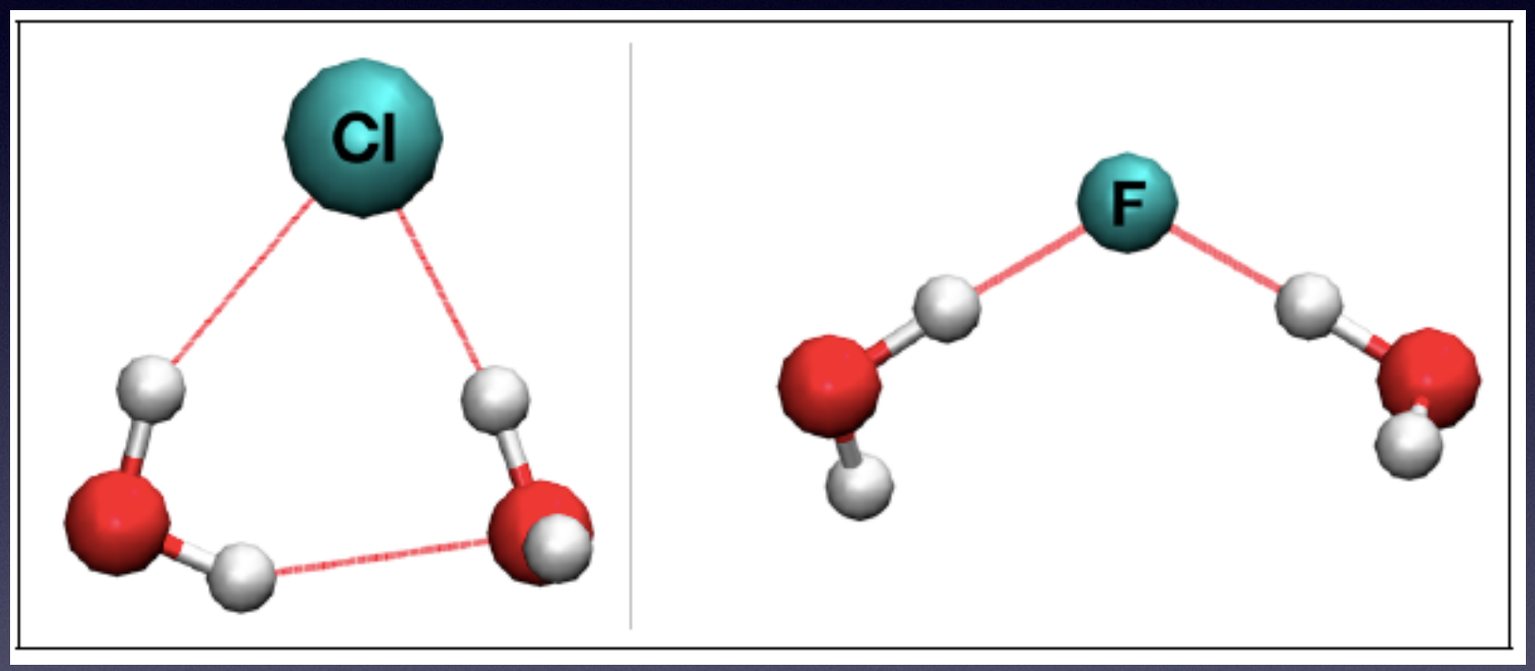
Dipole-rocking
dominates dynamics

$(H_2O)F^-$



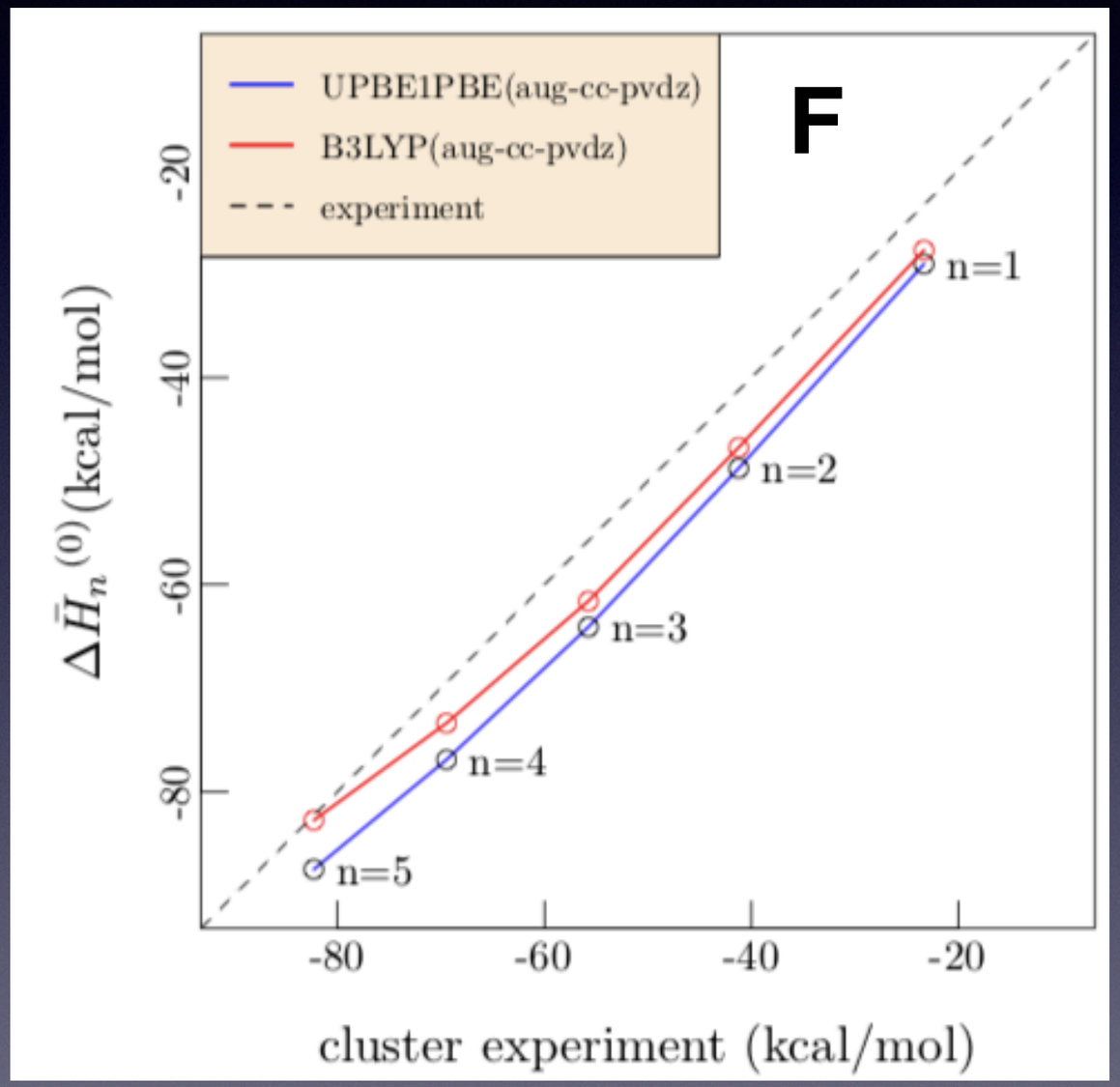
OH-F stretch
dominates dynamics

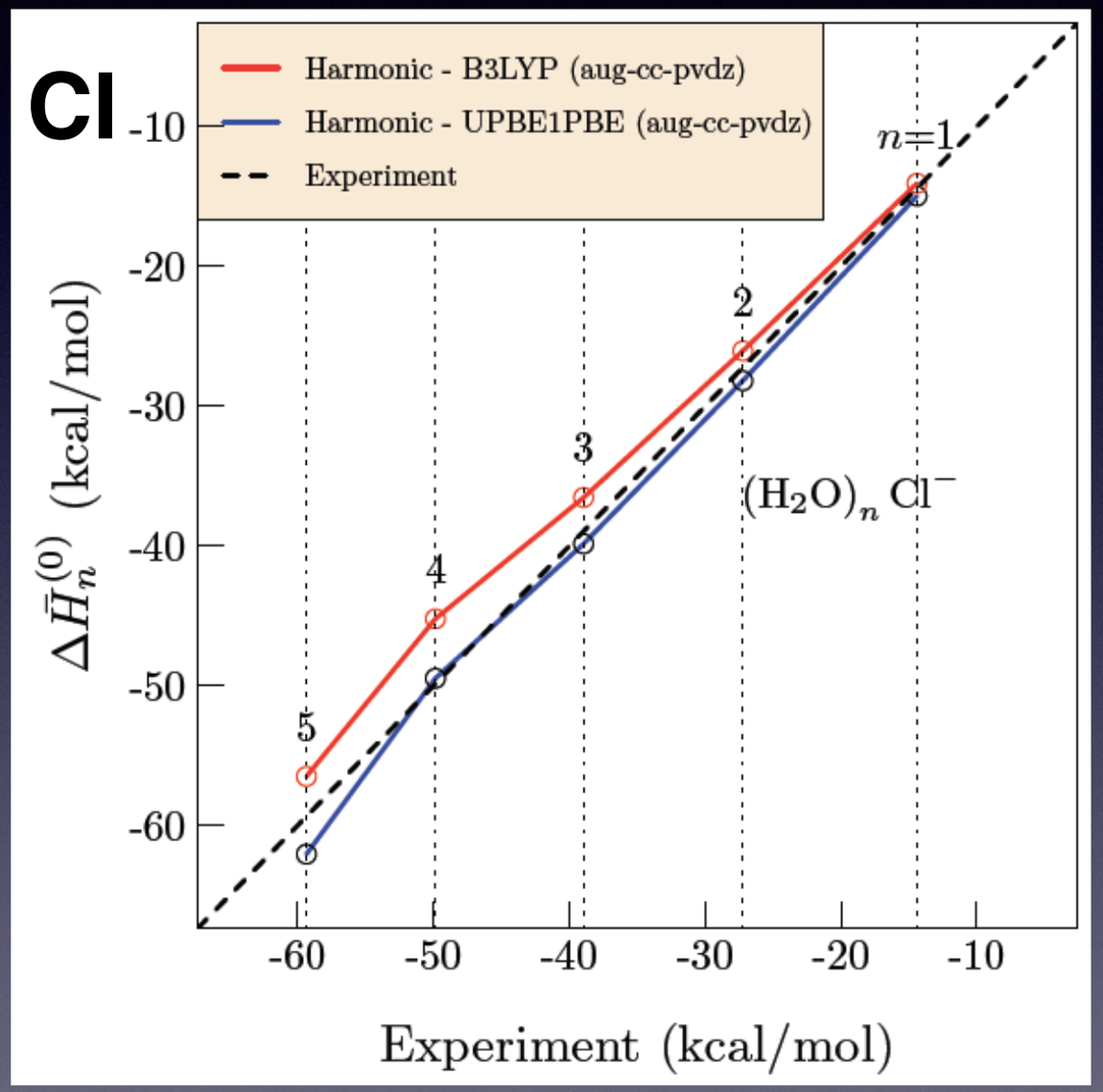
Different dynamics & structures (gas)



F ligands not H-bonded

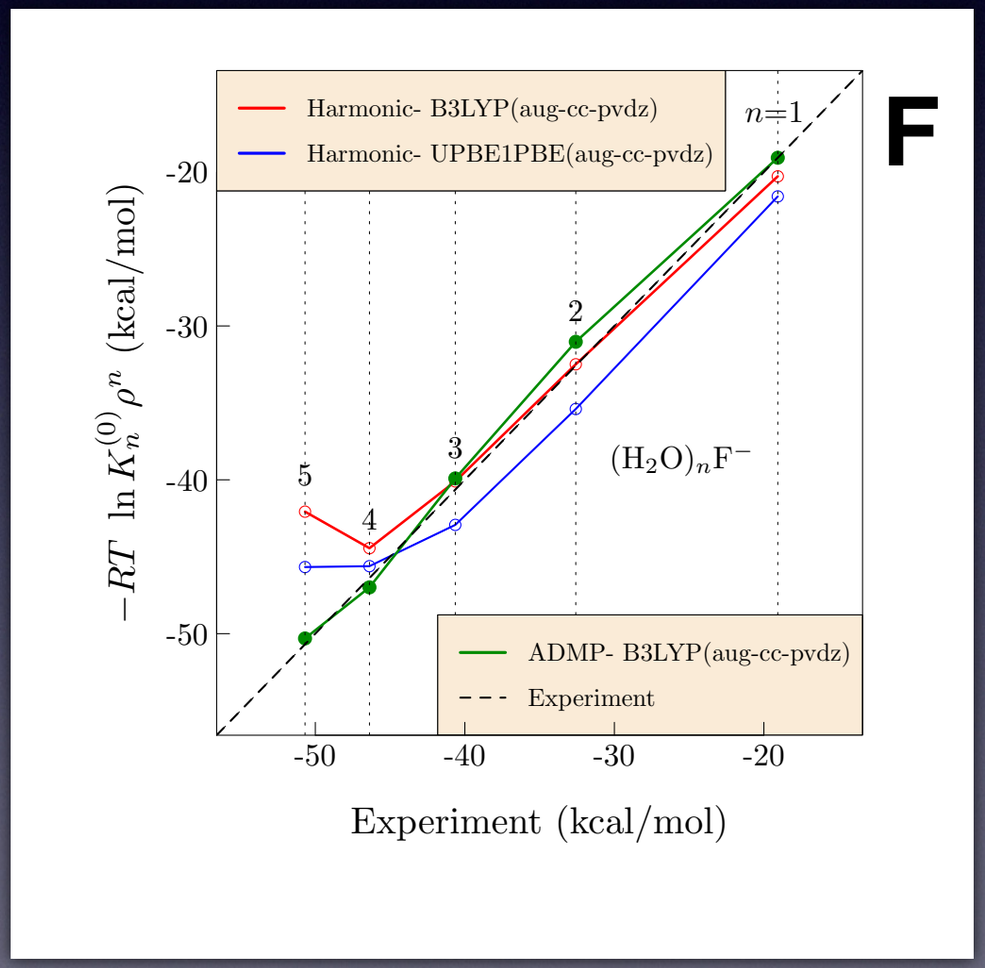
Harmonic approx. OK for enthalpy of clustering (gas)

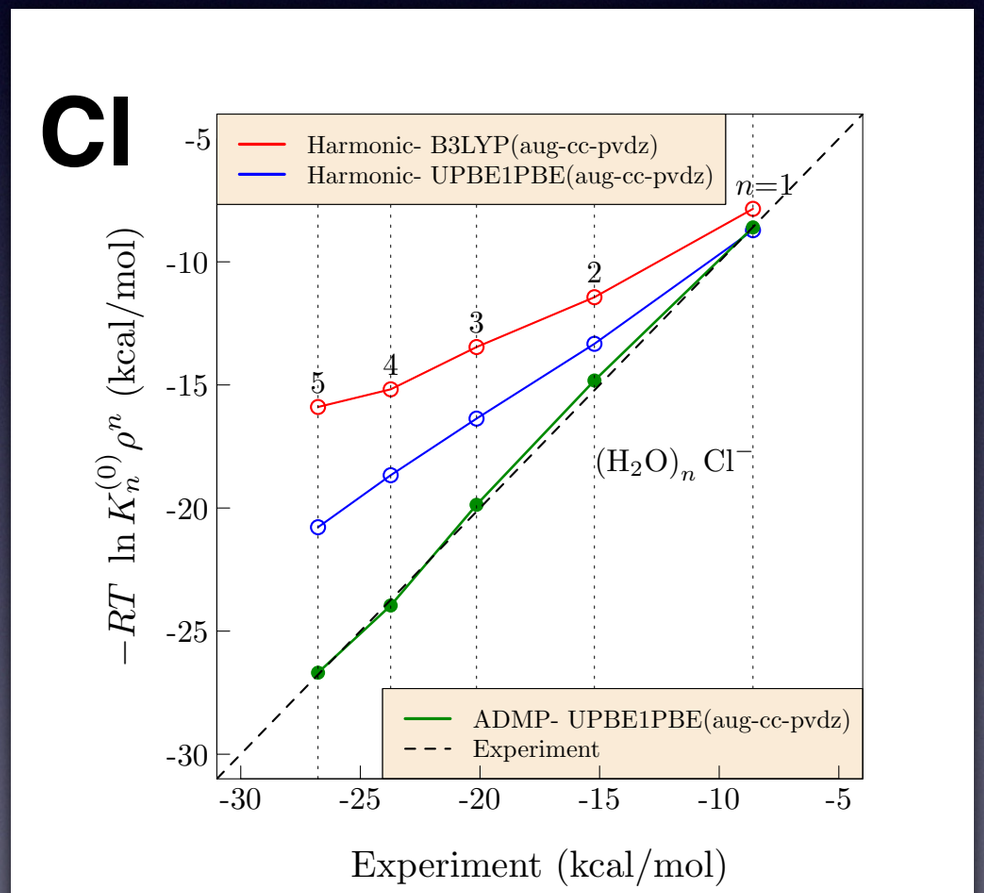




Strong chemical interactions (anion-ligand)

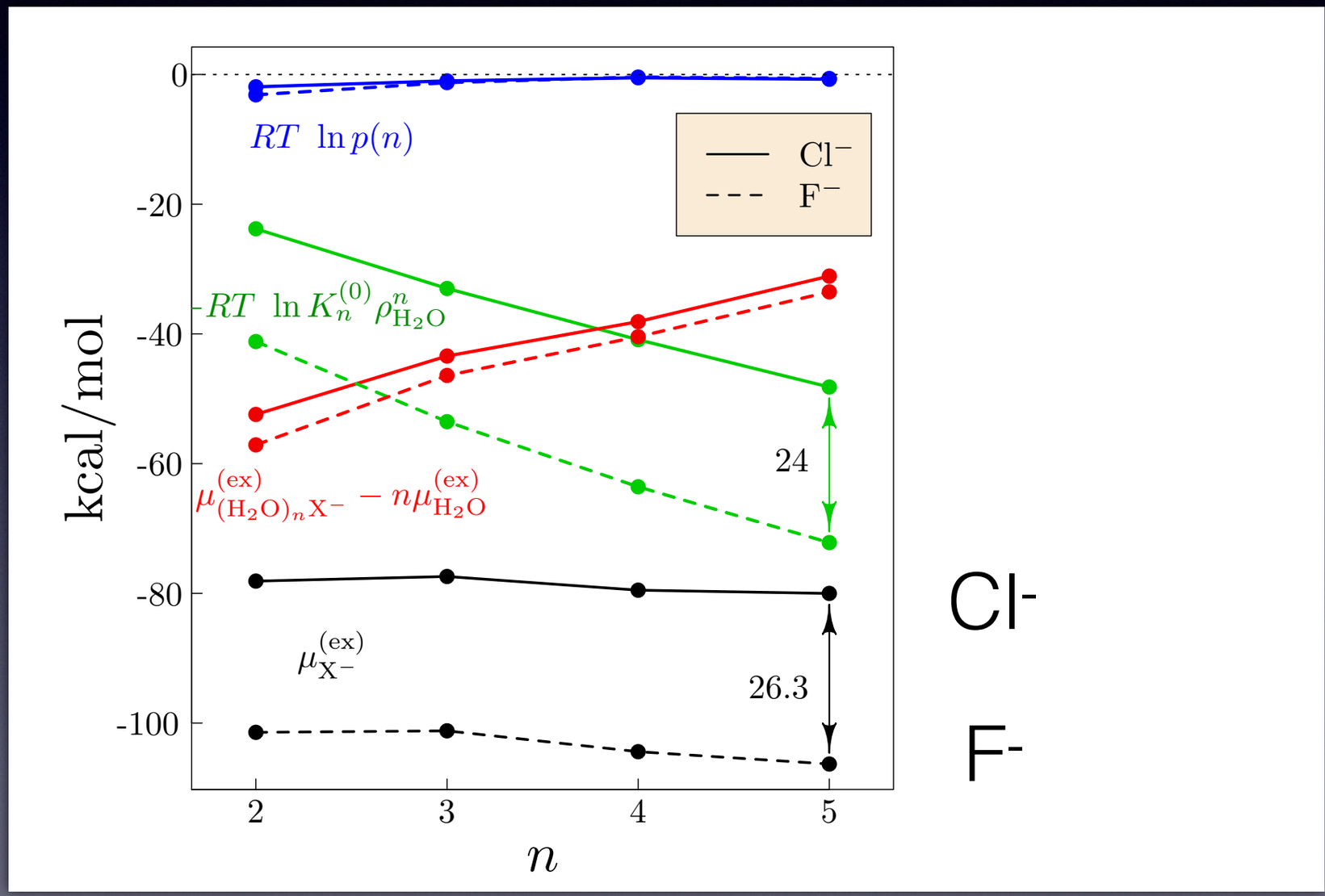
Anharmonicity needed for free E. of clustering (gas)





Especially for $Cl(H_2O)_{n>1}$ entropy component

Free energy differences due to local ion-water interactions (aq)

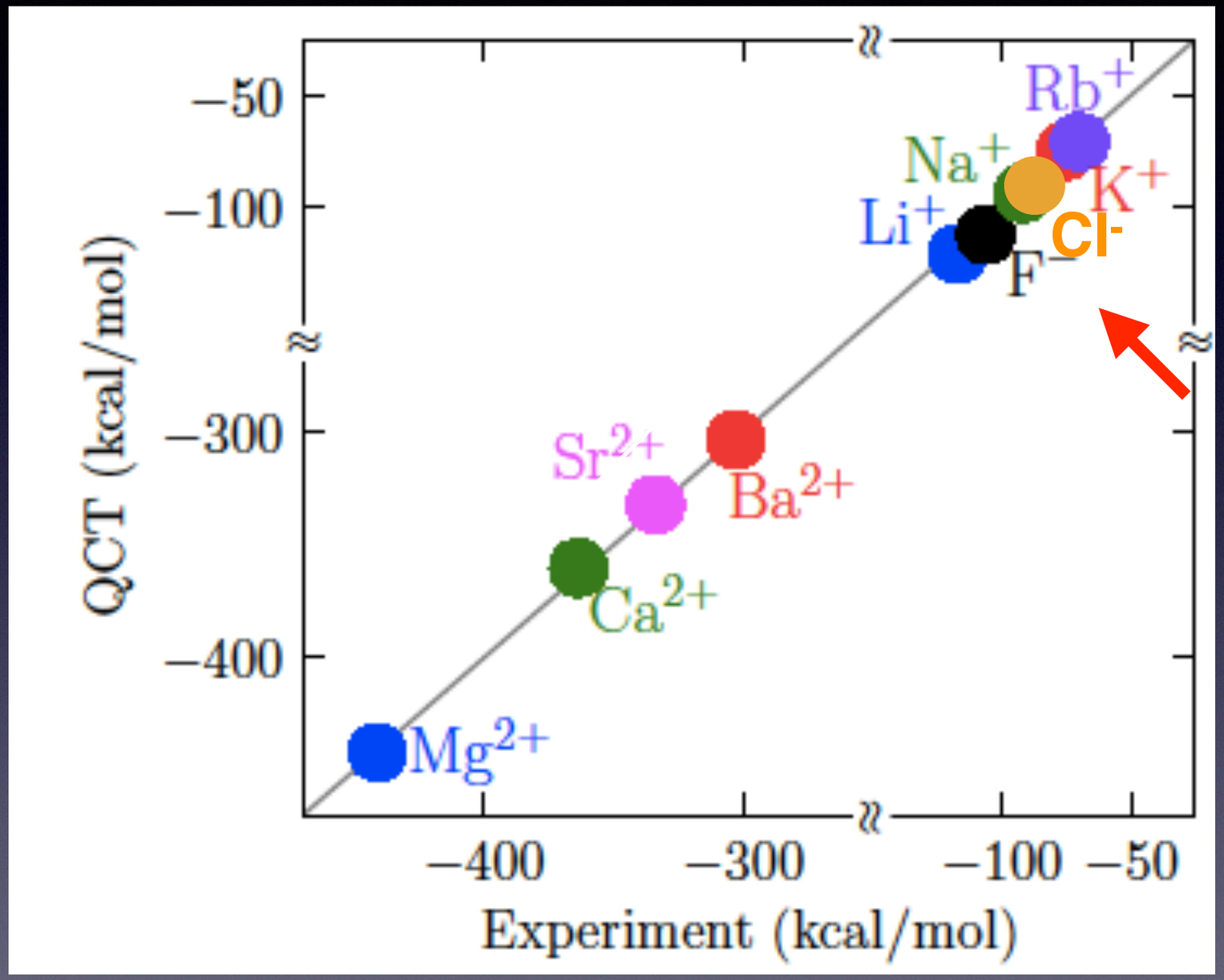


Cl-

F-

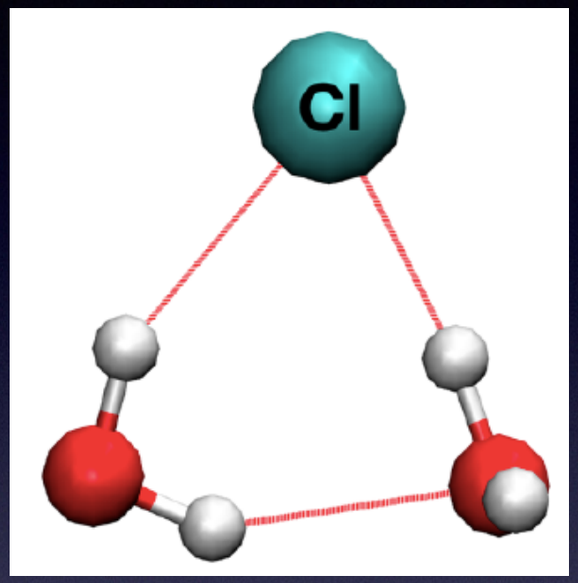
Independent of *n*, λ

QCT free energies

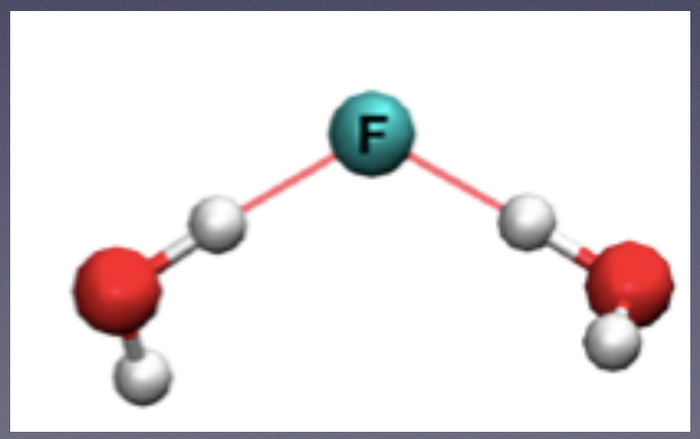


Cation & anion hydration agree with experiment

F^- & Cl^- story so far..

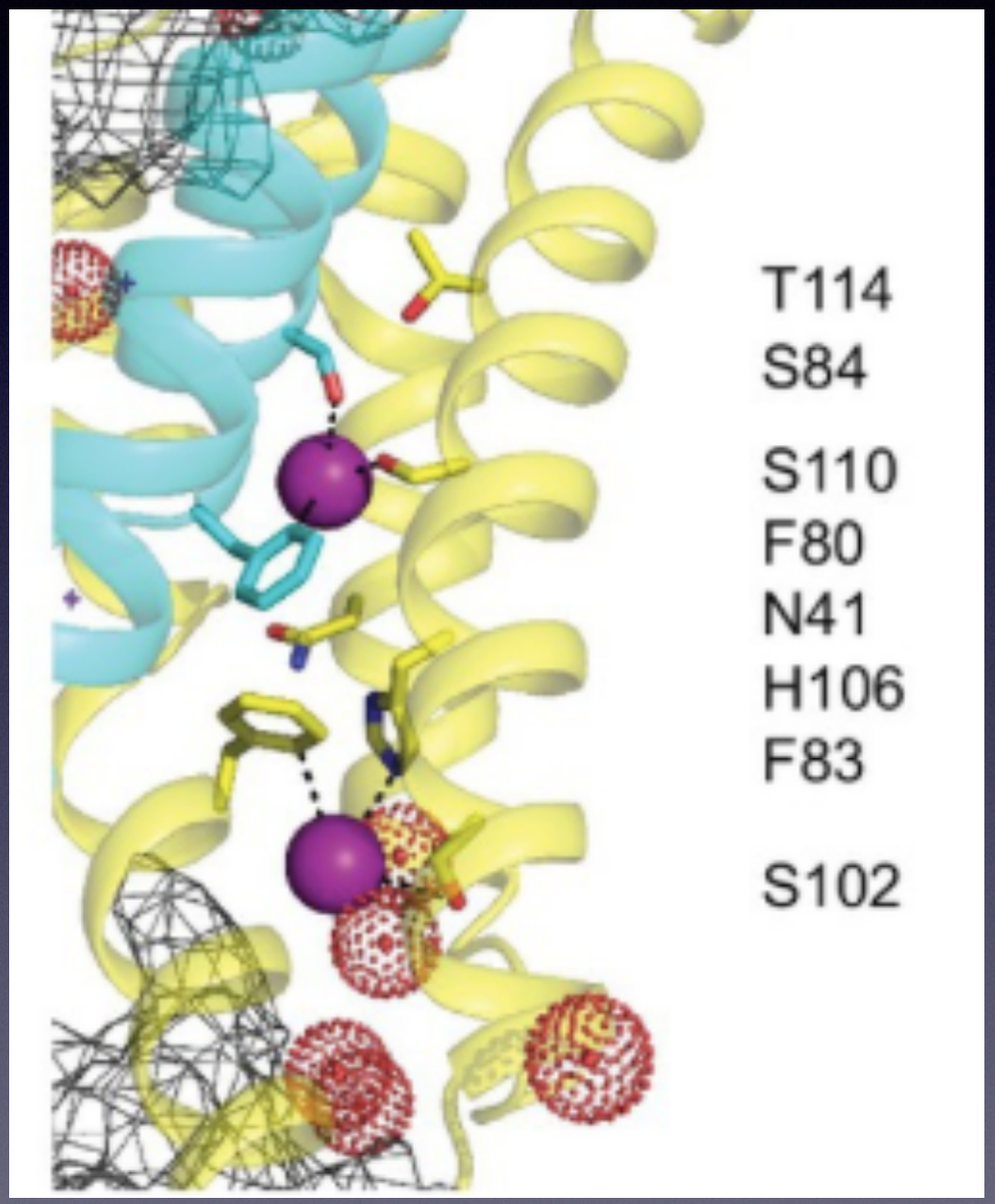


- Cl- larger (0.05 nm), looser ligands
- 4 waters define g(r) peak
- Dynamics dipole-rock dominated
- Anharmonic vibrations due to water-water H-bonds



- F- smaller, tighter ligands
- 4 waters define g(r) peak
- Dynamics F-OH stretch dominated.
- Harmonic vibrations.

Next, evaluate dynamic ion binding to Fluc channels…



2 F^- binding sites

Summary

- **QCT & molecular simulation predict cation & anion hydration (no fits).**
- Hydration is reference for ion channel permeation.
- Same number of waters define peaks in g(r) — 4
- Cl larger, ligated looser, cluster dynamics anharmonic & dipole-rock dominated.
- F smaller, ligated tighter, cluster dynamics harmonic & F-OH stretch dominated.

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