

Supporting Information

Calcium Ions in Aqueous Solutions: Accurate Force Field Description Aided by *Ab Initio* Molecular Dynamics and Neutron Scattering

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Acetate and formate force fields

Full description of the employed acetate and formate force fields (full charges and ECC) is provided in TABLE SI and TABLE SII.

TABLE SI. Details of the acetate CH_3COO^- force field, partial charges being provided both for the full charge and ECC description (the Lennard-Jones parameters are not changed in the ECC description).

atom	atom type	σ (Å)	ϵ (kJ/mol)	full charge (e)	ECC charge (e)
C1	C	3.39967	0.359824	+0.88641	+0.66481
O1	O2	2.95992	0.878640	-0.84114	-0.63086
O2	O2	2.95992	0.878640	-0.84114	-0.63086
C2	CT	3.39967	0.457730	-0.22228	-0.16671
H1	HC	2.64953	0.065689	+0.00605	+0.00454
H2	HC	2.64953	0.065689	0.00605	0.00454
H3	HC	2.64953	0.065689	0.00605	0.00454

TABLE SII. Details of the formate HCOO^- force field, partial charges being provided both for the full charge and ECC description (the Lennard-Jones parameters are not changed in the ECC description).

atom	atom type	σ (Å)	ϵ (kJ/mol)	full charge (e)	ECC charge (e)
C1	C	3.39967	0.359824	+0.81919	+0.61439
O1	O2	2.95992	0.878640	-0.81460	-0.61095
O2	O2	2.95992	0.878640	-0.81460	-0.61095
H1	H3	2.11499	0.065689	-0.18999	-0.14249

Sampled volume correction of the Ca^{2+} -formate free energy profiles

Free energy profiles for the calcium – formate ion pair were obtained using various restraints, therefore the standard isotropic volume correction cannot be employed. Instead, we approximated the accessible volume by the sampled volume, which was evaluated using the spherical coordinates defined in FIG. S1.

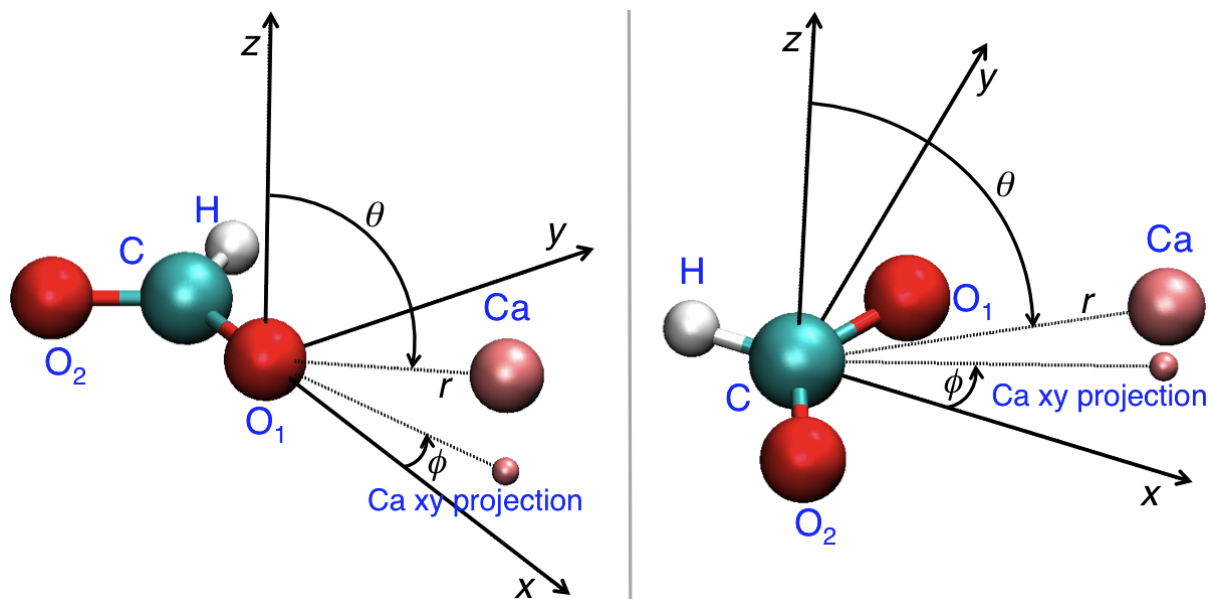


FIG. S1. Coordinate system used to calculate the sampled volume for umbrella sampling along the O-Ca distance (left) and along the C-Ca distance (right). The x and y axes lie in the formate plane.

For each bin in r , we separately determined the upper and the lower bounds of θ and ϕ so that at least 90 % of the sampled space is covered. Note that the distribution of ϕ for certain r exhibits more than one maximum. The sampled volume for each bin between r_1 and r_2 then reads:

$$V = 1/3 (r_2^3 - r_1^3) (-\cos(\theta_{\max}) + \cos(\theta_{\min})) \sum_i (\phi_{\max,i} - \phi_{\min,i}).$$

The bin width in r was 0.05 Å and $\pi/30$ for the angles. Finally, we smoothed the resulting r -dependence of V by running averages with the length of 5. The profiles are corrected by adding the $RT \ln(V/V(r(\text{SShIP})))$ term to the output of the WHAM algorithm, where $V(r(\text{SShIP}))$ is the sampled volume at the distance corresponding to the solvent shared ion pair, where the different profiles were aligned.

In order to show the influence of the sampled volume, we plot the uncorrected free energy profiles in FIG. S2. Comparison with FIG. 7 in the main text shows that omitting the correction would lead to shallower contact ion pair minimum and lower barrier for the ion pair dissociations.

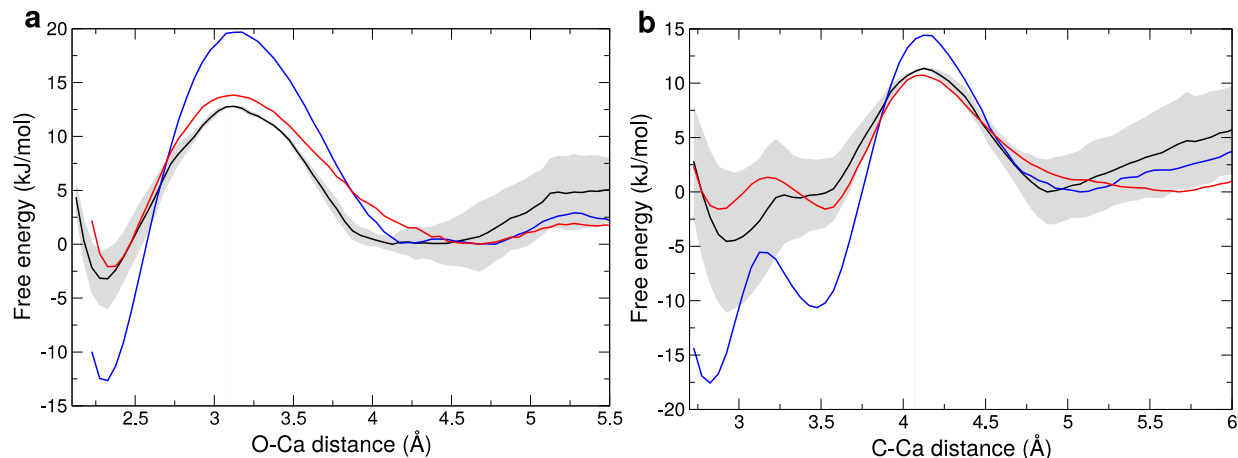


FIG. S2. Free energy profile without correction for the sampled volume along the Ca-O(formate) distance in a linear monodentate fashion and b) free energy profile along the C-Ca distance in the formate plane using AIMD (black), the full charges force field (blue) or a scaled charges force field both for calcium and formate (red).

The procedure for the correction of the 2D free energy landscape is analogous, with upper and lower bounds of the sampled θ and ϕ angles determined for each $(r, \text{Ca-C-O}_{\text{mid}})$ bin.

Ca(H₂O)₆²⁺ clusters geometry optimization at different levels of theory

To assess the sensitivity of the Ca-O(water) distance with respect to the employed level of theory, we optimized the geometry of a perfectly symmetric Ca(H₂O)₆²⁺ cluster at different level of theory up to CCSD(FULL) level and with different basis sets up to cc-pVTZ. The Ca-O distance in the optimized clusters, either in the gas phase or with a continuum solvent model, PCM, is summarized in TABLE III.

TABLE III. Ca-O distances in a Ca(H₂O)₆²⁺ cluster optimized with different level of theory and basis sets.

Method	Basis set	Ca-O distance (Å) (gas phase)	Ca-O distance (Å) (water PCM)
BLYP-D2	6-31G*	2.42	2.42

	6-311++G**	2.41	2.41
	cc-pVTZ	2.40	2.40
B3LYP	6-31G*	2.42	2.42
	6-311++G**	2.40	2.40
	cc-pVTZ	2.40	2.40
MP2 (FULL)	6-31G*	2.43	2.42
	6-311++G**	2.38	2.41
	cc-pVTZ	2.38	2.40
CCSD (FULL)	6-31G*	2.43	2.42
	6-311++G**	2.38	2.40

Additional comparisons for the Ca-Cl free energy profile

In FIG. S3, we compare the *ab initio* free energy profile obtained in the present work with that obtained independently in Ref¹, using exactly the same setup. They are clearly consistent within the estimated error bars of the calculation, which suggests that this profile is well converged, despite the relatively short simulation times.

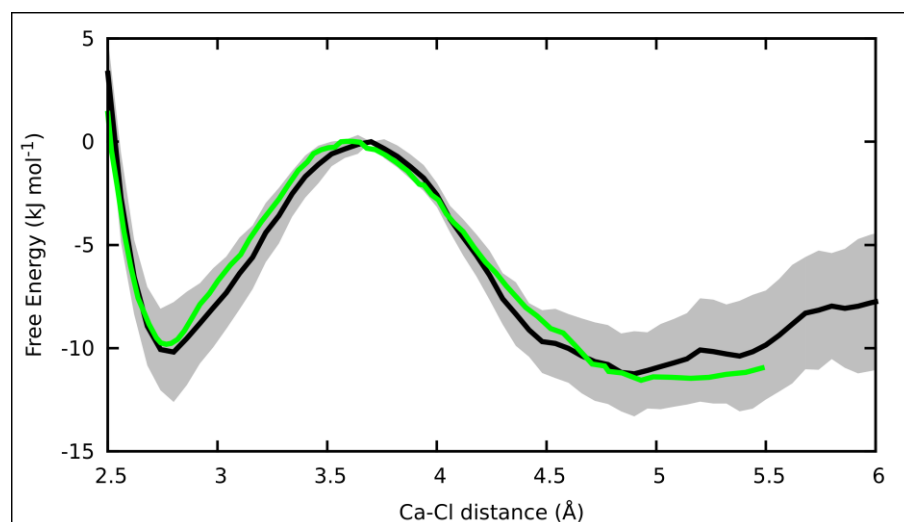


FIG. S3. AIMD free energy profile along the Ca-Cl distance as obtained in the present work (black) and independently by Baer and Mundy with the same setup¹ (green).

FIG. S4 compares the free energy profile obtained with the ECCR2 force field with both the AIMD result and the profile obtained using a fully polarizable force field, AMOEBA^{2,3}. AMOEBA09 parameters are employed with

parameters for Ca^{2+} taken from⁴. The free energy profiles obtained with the three different methods are extremely similar. This underlines the quality of the new ECCR2 force field, which performs equally well as a fully polarizable one.

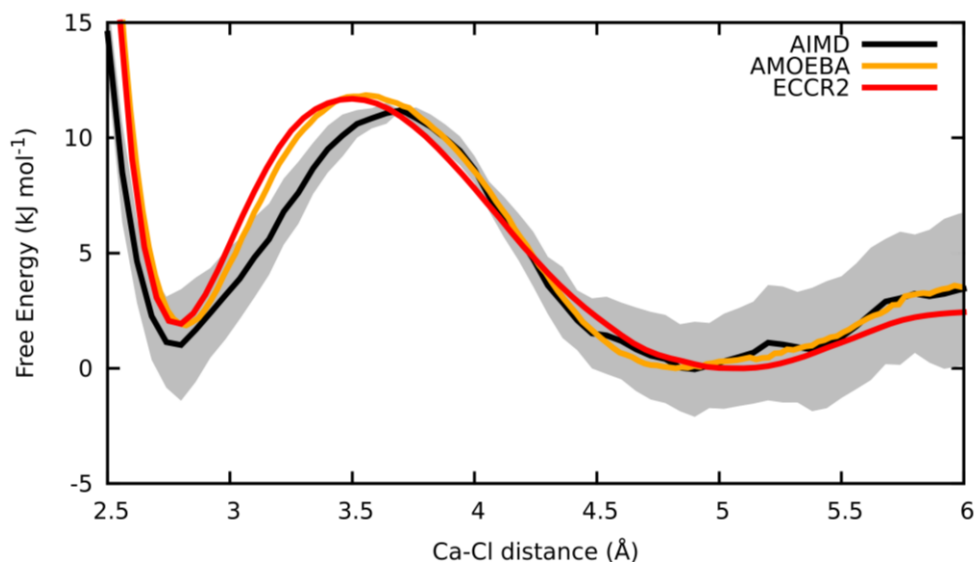


FIG. S4. Free energy profile along the Ca-Cl distance computed at the AIMD level (black), using the fully polarizable AMOEBA force field (orange) and the ECCR2 force field introduced in the present work.

Force field sensitivity of the Ca-carboxylate interaction

We compared the behavior of our two scaled charges calcium force fields (the original ECCR and the newer ECCR2 developed in the present work). Both descriptions provide very similar (less than 0.5 kJ/mol difference) free energy differences between the CIP and SShIP for the monodentate interaction with a formate group (FIG. S5) and similar barriers between the two states (within 2 kJ/mol). In addition, FIG. S6 shows that the overall structure of a concentrated calcium acetate solution compared with neutron scattering data is very well described by both force fields (FIG. S6 with ECCR and FIG. 5 in main text with ECCR2). The differences between the two descriptions are minimal, which means that the description of ion pairing is very similar with both force fields.

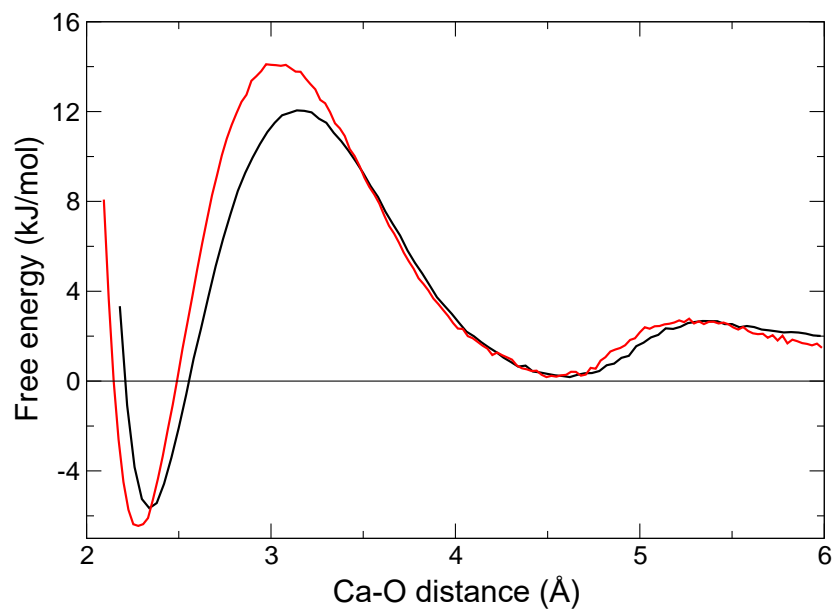


FIG. S5. Free energy profile along the Ca-O(formate) distance in a linear monodentate fashion, using scaled charges (ECC) description for formate and the ECCR2 (black) or ECCR (red) force field for calcium.

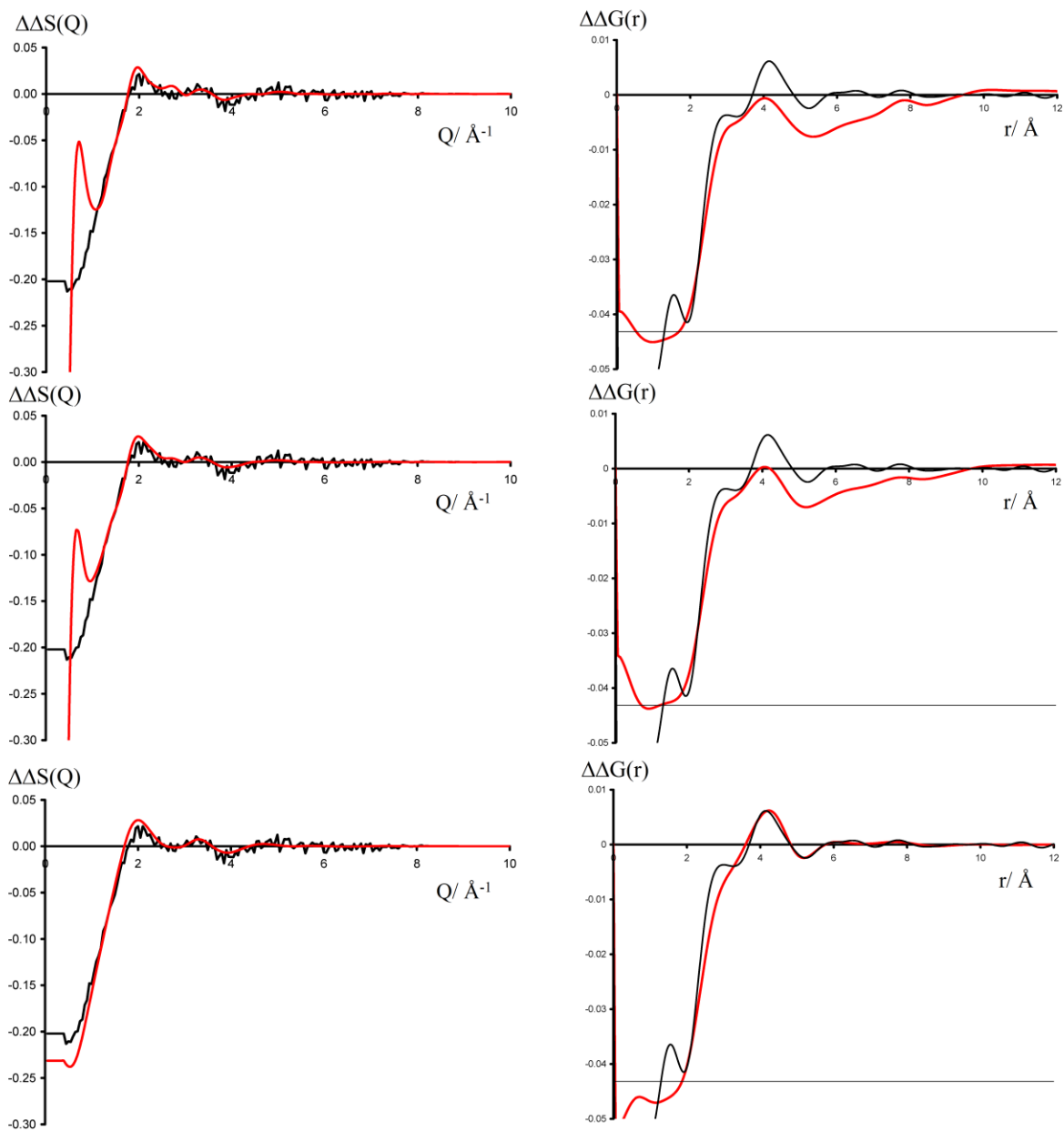


FIG. S6. Comparison between the experimental neutron double difference (black) in Q space, $\Delta\Delta S(Q)$ (left), and in r space, $\Delta\Delta G(r)$ (right), and the signal calculated from molecular dynamics simulations (red) using a) a full charges force field, b) the ECCR force field for Ca^{2+} and full charges for the acetate and c) the ECCR force field for Ca^{2+} and a ECC description for the acetate anion.

REFERENCES

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