FORCE-FIELD INDEPENDENT METAL PARAMETERS USING A NON-BONDED DUMMY MODEL

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Table of content

Table S1: A comparison of calculated and observed solvation free energies (ΔG_{hyd}, kcal/mol), and ion-water oxygen distances (M^{2+}-O, Å) for Zn^{2+}, Ca^{2+} and Mg^{2+} soft-sphere models employing parameters developed by Stote and Karplus[1] and Åqvist[2] [a].

					TIP3P		Experimental	
	e	$\mathbf{A_i^M}$	$\mathbf{B_i^M}$	$\mathbf{m^M}$	$\mathbf{\Delta G_{hyd}}$	$\mathbf{M^{2+}\text{-}O^a}$	$\mathbf{\Delta G_{hyd}}$[3]	$\mathbf{M^{2+}\text{-}O}$[4]
ZN[b]	2.0	54.98	7.42	65.4	-443.5±0.2	2.05±0.06	-483.3	2.08
MG	2.0	96.0	32.0	24.3	-449.2±0.1	2.08±0.05	-454.2	2.10
CA	2.0	264.1	18.82	40.1	-386.7±0.2	2.38±0.01	-379.5	2.39-2.46[5, 6]

[a]All values are averages and standard deviations over 5 trajectories, as outlined in the main text. M-O distances for all the water molecules bound to the metal were monitored along the simulations with sampling every 0.5 ps, and averages over the entire simulation are presented here. With the exception of Ca^{2+}, which shows a rapid water exchange, the M-O distance was directly taken from the peak of the RDF (see Figure S1). [b] The original Stote and Karplus parameters[1], σ(Å)=1.95 and ε(kcal/mol)=0.25, were converted using the following expression $A=\sqrt{4\varepsilon(\sigma)^{12}}$ and $B=\sqrt{4\varepsilon(\sigma)6}$.

Figure S1: Radial distribution functions (*g(r), y_1-axis*) and coordination number (N[*g(r)*], y_2-axis) corresponding to the first hydration shell of (A) Zn^{2+}, (B) Ca^{2+}, and (C) Mg^{2+}obtained using the soft-sphere models parameters presented in Table S1. In all cases, the M^{2+}-O *g(r)* are represented by solid lines and the N[*g(r)*] by dashed lines.

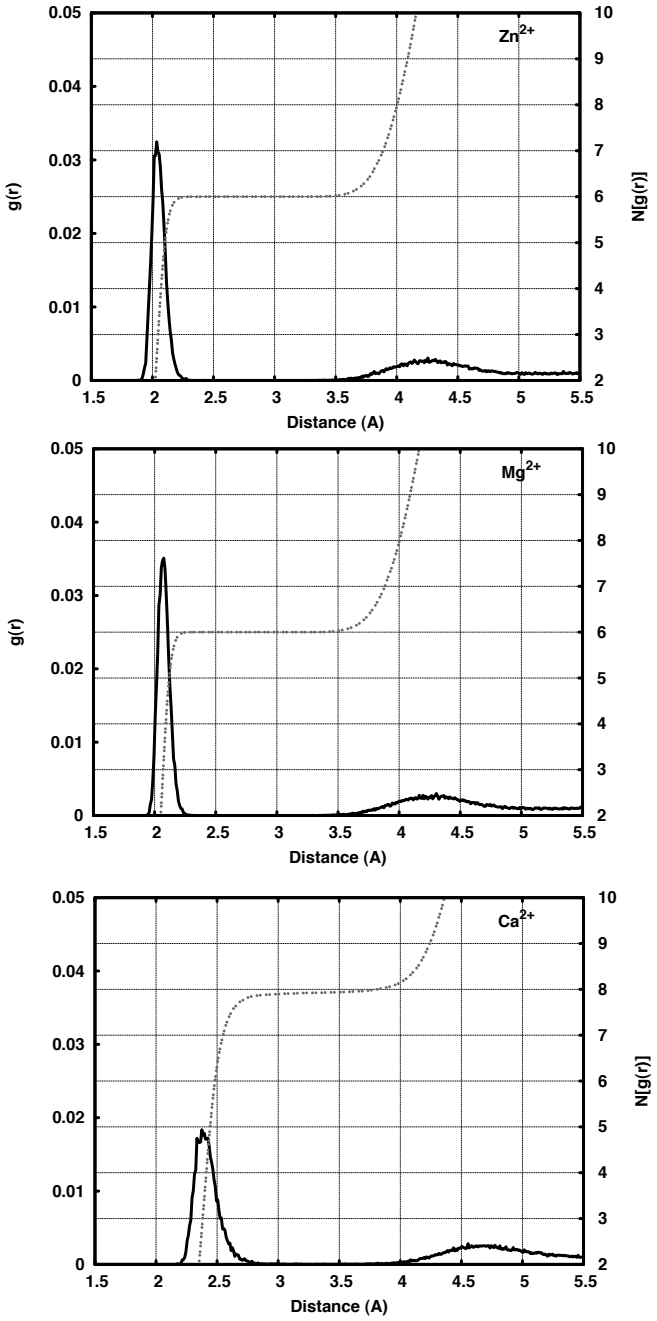


Figure S2: Radial distribution functions (*g(r), y_1-axis*) and coordination number (N[*g(r)*], y_2-axis) corresponding to the first hydration shell of (A) Ca^{2+} dummy model from Sept *et al*[7] and (B) the new Ca^{2+}-dummy model presented in this work.

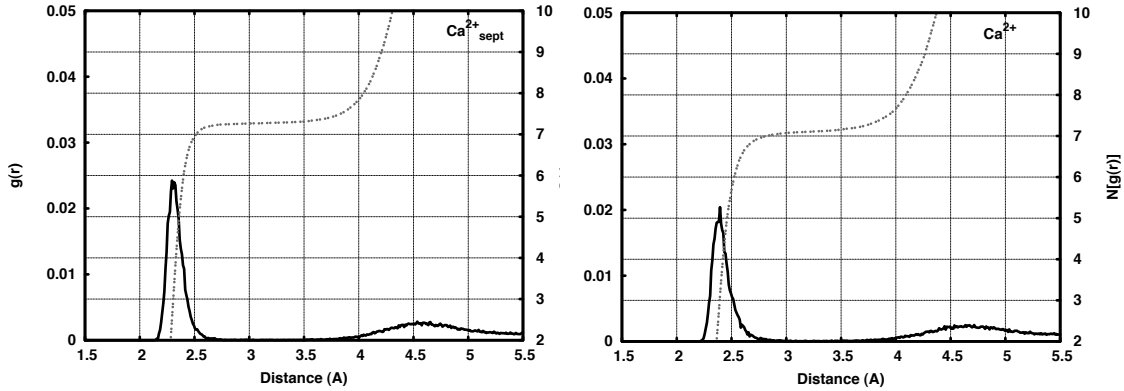
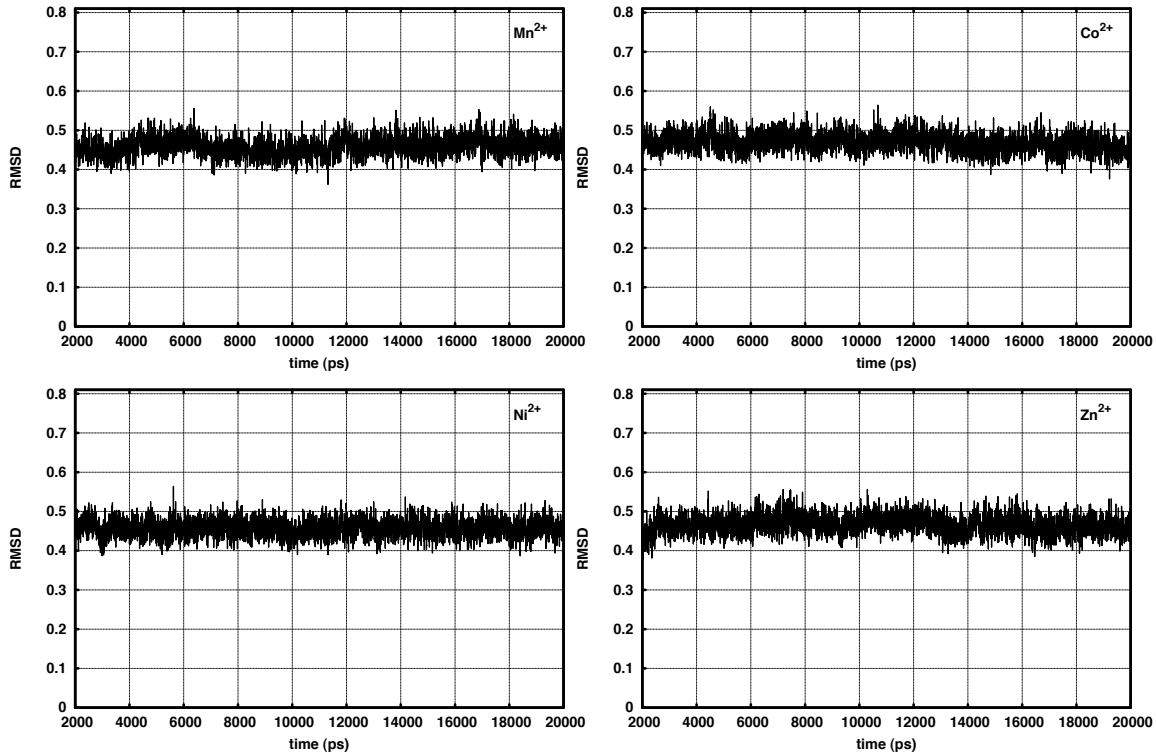
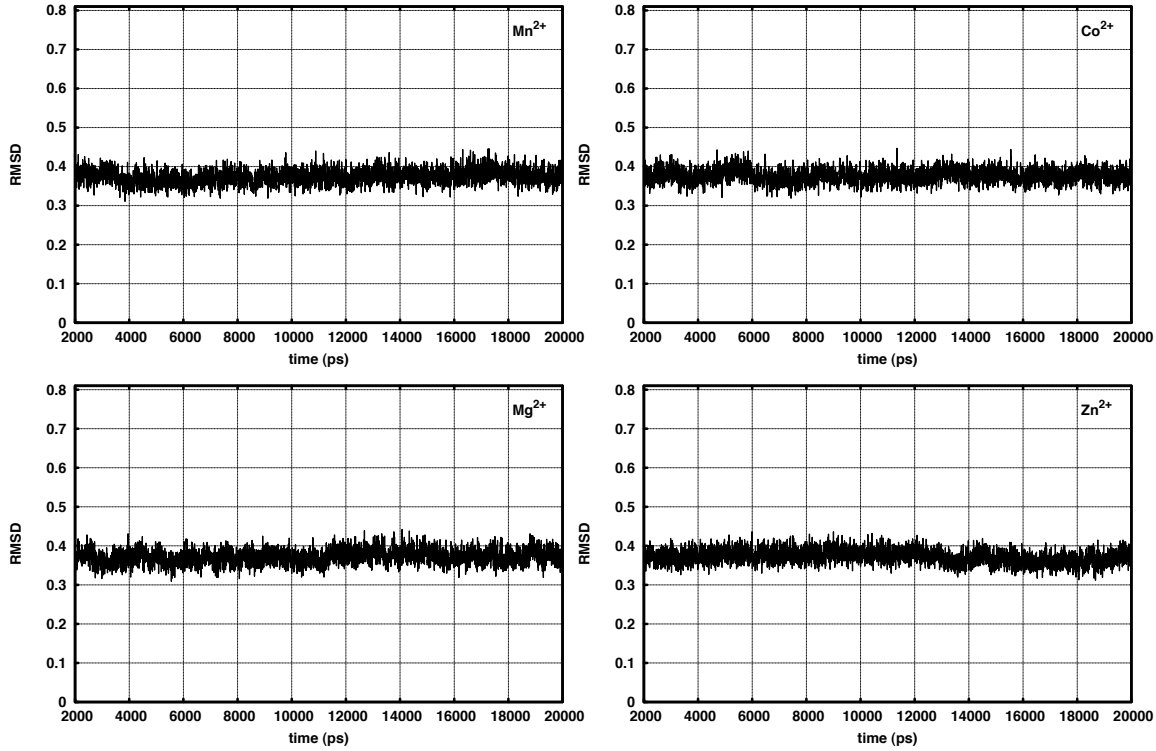


Figure S3: Time-averages of the root mean square deviation (in Å) of the protein backbone atoms ($RMSD_{backbone}$)[a] for *E.coli* Glyoxalase with different metals.



[a]RMSD for the protein backbone have been calculated taken into account only the atoms within 20Å of the system center, i.e those that are inside the solvent sphere and are not subject to any restraint apart from the weak 0.1kcal/mol harmonic restraint mentioned in the main text.

Figure S4: Time-averages of the root mean square deviation (in Å) of the protein backbone atoms ($RMSD_{backbone}$) for *Human* GlxI with different metals[a].



[a]RMSD for the protein backbone have been calculated taken into account only the atoms within 20Å of the system center, i.e those that are inside the solvent sphere and are not subject to any restraint apart from the weak 0.1kcal/mol harmonic restraint mentioned in the main text.

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