Electronic Supplementary Information

Systematic Evaluation of Bundled SPC Water for Biomolecular Simulations

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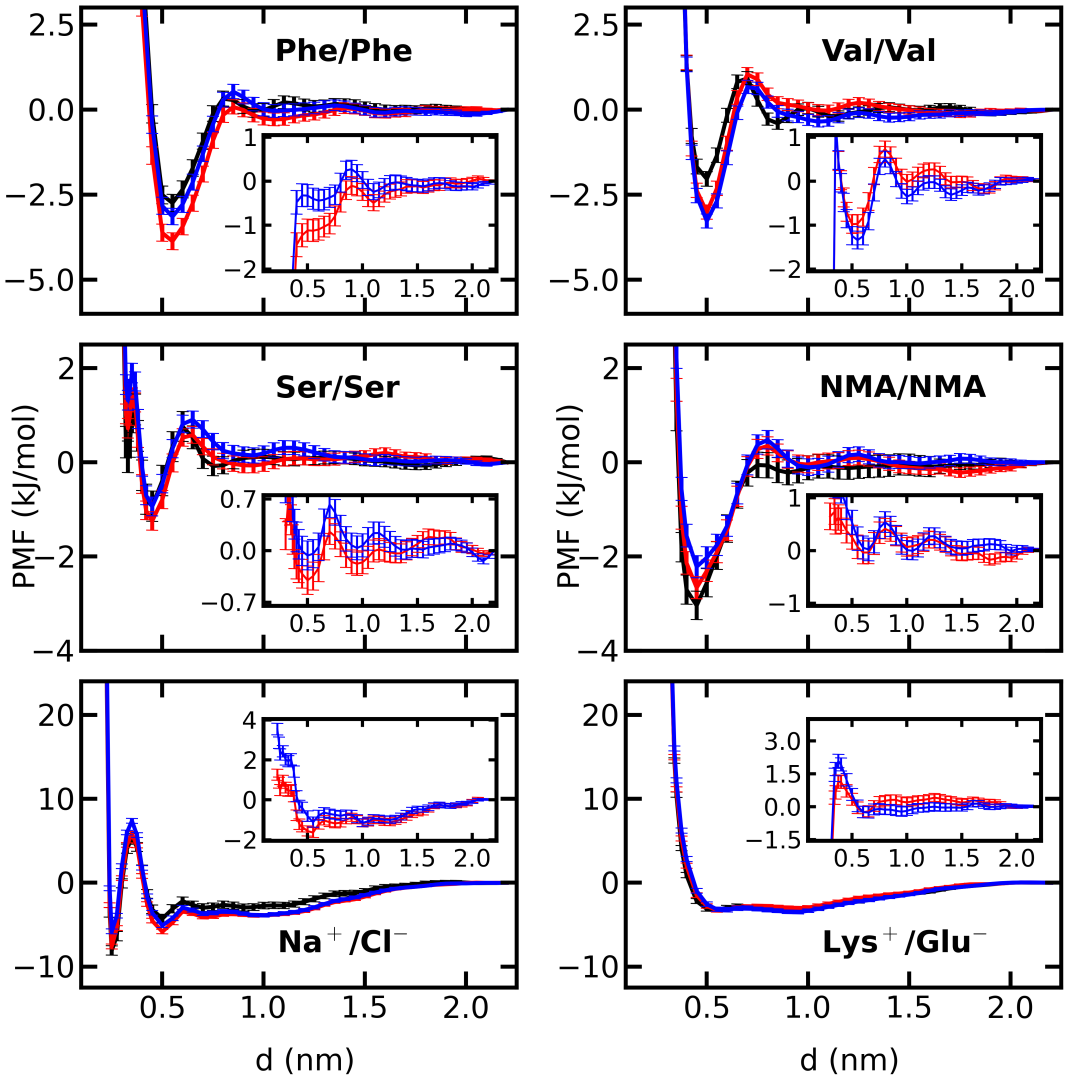


ESI Figure 1: PMFs in bundled SPC (red and blue curves for MOD1 and MOD2, respectively) as compared to the reference PMFs in unrestrained SPC/E (black). Insets show the deviation from the reference.

aminoacid	ΔG_{hyd} (kJ/mol)			
	Expt.	SPC	MOD1	MOD2
ala	8.1	8.3 (0.1)	8.9 (0.6)	8.4 (0.7)
asn	-40.5	-43.1 (0.3)	-45.3 (1.2)	-47.4 (1.2)
cys	-5.2	-6.1 (0.2)	-6.3 (0.8)	-7.7 (0.8)
gln	-39.2	-42.3 (0.3)	-44.6 (1.5)	-46.9 (1.3)
leu	9.5	9.7 (0.3)	9.3 (1.1)	7.8 (1.0)
met	-6.2	-9.9 (0.3)	-9.5 (1.2)	-10.6 (1.1)
phe	-3.2	-2.0 (0.3)	-1.9 (1.3)	-3.6 (1.8)
ser	-21.2	-23.4 (0.3)	-24.4 (1.0)	-25.3 (1.1)
thr	-20.4	-22.1 (0.3)	-22.5 (1.3)	-24.0 (1.2)
trp	-24.6	-26.6 (0.4)	-28.2 (1.6)	-30.9 (1.5)
tyr	-25.6	-26.9 (0.4)	-28.7 (1.7)	-31.3 (1.5)
val	8.3	7.8 (0.2)	8.5 (1.1)	7.6 (1.0)

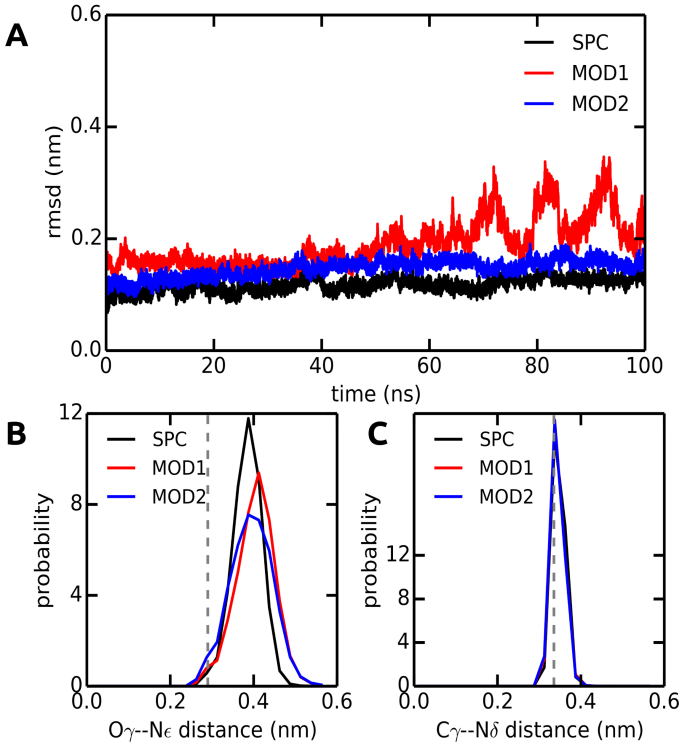
ESI Table 1: Calculated values of ΔG_{hyd} in unrestrained SPC (Hess et al, J. Phys. Chem. B, 2006), MOD1 and MOD2 compared to experiment (Wolfenden et al, Biochemistry, 1981). Statistical errors are indicated in brackets.

aminoacid	ΔH_{hyd} (kJ/mol)			
	Expt.	SPC	MOD1	MOD2
ala	-8.3	-3.2 (0.8)	-0.3 (1.4)	0.8 (1.1)
asn	-67.0	-66.9 (0.7)	-74.5 (1.4)	-76.2 (0.8)
cys	-23.9	-22.4 (0.8)	-21.5 (1.4)	-22.5 (0.8)
gln	-70.4	-69.9 (0.7)	-75.8 (0.9)	-77.3 (1.1)
leu	-17.1	-11.9 (0.8)	-4.3 (1.4)	-4.3 (0.7)
met	-34.6	-32.2 (0.8)	-29.3 (0.8)	-30.8 (1.0)
phe	-25.3	-27.9 (0.8)	-24.4 (1.1)	-24.9 (1.1)
ser	-43.0	-45.0 (0.8)	-48.4 (1.5)	-49.0 (1.5)
thr	-45.0	-49.4 (0.8)	-47.3 (0.8)	-47.9 (0.6)
trp	-58.8	-58.2 (0.8)	-58.5 (0.7)	-59.4 (0.9)
tyr	-57.4	-62.8 (0.8)	-64.5 (1.1)	-65.3 (0.8)
val	-13.7	-10.5 (0.8)	-6.1 (1.2)	-5.1 (1.2)

ESI Table 2: Calculated values of ΔH_{hyd} in unrestrained SPC (Hess et al, J. Phys. Chem. B, 2006), MOD1 and MOD2 compared to experiment (Makhatadze et al, J. Mol. Biol. 1993). Statistical errors are indicated in brackets.

aminoacid	$T\Delta S_{hyd}$ (kJ/mol)			
	Expt.	SPC	MOD1	MOD2
ala	-16.4	-11.5 (0.8)	-9.2 (1.5)	-7.6 (1.3)
asn	-26.5	-23.8 (0.8)	-29.2 (1.8)	-28.8 (1.4)
cys	-18.7	-16.3 (0.8)	-15.2 (1.6)	-14.8 (1.1)
gln	-31.2	-27.6 (0.8)	-31.2 (1.7)	-30.4 (1.7)
leu	-26.6	-22.9 (0.9)	-13.9 (1.8)	-11.8 (1.2)
met	-28.4	-22.3 (0.9)	-19.8 (1.4)	-20.2 (1.5)
phe	-22.1	-25.9 (0.9)	-22.5 (1.7)	-21.3 (2.1)
ser	-21.8	-21.6 (0.9)	-24.0 (1.8)	-24.7 (1.9)
thr	-24.6	-27.3 (0.8)	-24.8 (1.5)	-23.9 (1.3)
trp	-34.2	-31.6 (0.9)	-30.2 (1.7)	-28.4 (1.7)
tyr	-31.8	-35.9 (0.8)	-35.8 (2.0)	-33.4 (1.7)
val	-22.0	-18.9 (0.8)	-14.6 (1.6)	-12.7 (1.6)

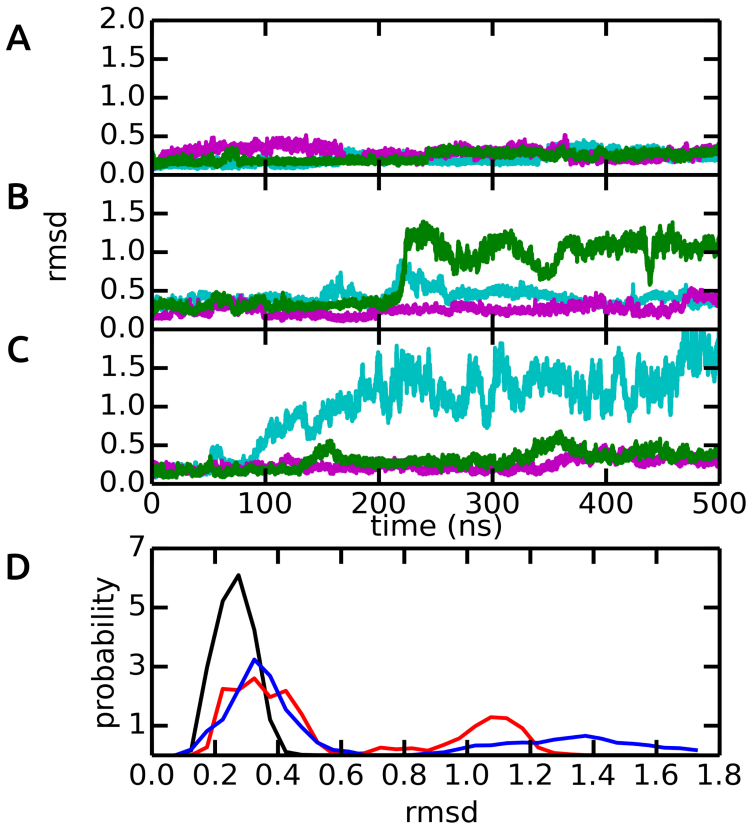
ESI Table 3: $T\Delta S_{hyd} = \Delta H_{hyd} - \Delta G_{hyd}$ in unrestrained SPC, MOD1 and MOD2. Errors are shown in brackets.



ESI Figure 2: Comparison of structural parameters of $\alpha - \mathrm{CT}$ in unrestrained SPC (black), MOD1 (red) and MOD2 (blue) with Amber (99sb-ildn) force field. (A) Backbone RMSD. (B) Distribution of Ser-195 Oγ – His-57 Nϵ distance. (C) Distribution of ASP-102 Cγ – His-57 Nδ distance. Dashed gray line shows the distances seen in X-ray structure.

ESI Table 4: Average number of waters in $\alpha - \mathrm{CT}$ active site and hydrogen bonds between water and catalytic triad residues with Amber (99sb-ildn) force field.

	# water	# hbonds					
		Ser-195		Asp-102		His-57	
		backbone	sidechain	backbone	sidechain	backbone	sidechain
X-ray	4.0	1.0	1.0	1.0	–	1.0	–
SPC	3.6 (0.4)	0.0	1.4 (0.0)	0.8 (0.0)	0.4 (0.5)	1.5 (0.0)	1.1 (0.1)
MOD1	5.8 (0.2)	0.9 (0.0)	2.0 (0.0)	0.6 (0.4)	1.4 (0.1)	1.4 (0.0)	0.7 (0.0)
MOD2	5.2 (0.7)	0.9 (0.0)	1.9 (0.0)	0.6 (0.4)	1.1 (0.5)	1.4 (0.0)	0.9 (0.0)



ESI Figure 3: Comparison of backbone RMSD of the coiled-coil dimer in (A) unrestrained SPC, (B) MOD1 and (C) MOD2. Three independent runs are shown for each solvent. (D) Distribution of RMSD over last 200 ns from the above simulations in SPC (black), MOD1 (red) and MOD2 (blue).