Variational Optimization of an All-Atom EEF1 Implicit Solvent to Match Explicit Solvent Simulation Data

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Supporting Information

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Table 1: Solvation parameters used in EEF1-SB. The volume (in Å^3) is given by the van der Waals volume minus the overlap with the volume of covalently bonded atoms. The values of ΔG^{ref} (kcal mol^{-1}), ΔH (kcal mol^{-1}), and ΔC_{p} (kcal mol^{-1} K^{-1}) are taken from the original EEF1 model. The correlation length λ is 3.5 Å , except for atoms in ionic groups, for which a value of $\lambda = 6$ Å is used.

Atom type	Volume	ΔG^{ref}	ΔG^{free}	ΔH	ΔC_{p}	λ
C	14.720	0.000	0.000	0.000	0.0	3.5
CD	14.720	0.000	0.000	0.000	0.0	3.5
CT1	11.507	-0.187	-0.187	0.876	0.0	3.5
CT2	18.850	0.372	0.372	-0.610	18.6	3.5
CT2A	18.666	0.372	0.372	-0.610	18.6	3.5
CT3	27.941	1.089	1.089	-1.779	35.6	3.5
CPH1	5.275	0.057	0.080	-0.973	6.9	3.5
CPH2	11.796	0.057	0.080	-0.973	6.9	3.5
CPT	4.669	-0.890	-0.890	2.220	6.9	3.5
CY	10.507	-0.890	-0.890	2.220	6.9	3.5
CP1	25.458	-0.187	-0.187	0.876	0.0	3.5
CP2	19.880	0.372	0.372	-0.610	18.6	3.5
CP3	26.731	0.372	0.372	-0.610	18.6	3.5
CC	16.539	0.000	0.000	0.000	0.0	3.5
CAI	18.249	0.057	0.057	-0.973	6.9	3.5
CA	18.249	0.057	0.057	-0.973	6.9	3.5
N	0.000	-1.000	-1.000	-1.250	8.8	3.5
NR1	15.273	-5.950	-5.950	-9.059	-8.8	3.5
NR2	15.111	-3.820	-3.820	-4.654	-8.8	3.5
NR3	15.071	-5.950	-5.950	-9.059	-8.8	3.5
NH1	10.197	-5.950	-5.950	-9.059	-8.8	3.5
NH2	18.182	-5.950	-5.950	-9.059	-8.8	3.5
NH3	18.817	-20.000	-20.000	-25.000	-18.0	6.0
NC2	18.215	-10.000	-10.000	-12.000	-7.0	6.0
NY	12.001	-5.950	-5.950	-9.059	-8.8	3.5
NP	4.993	-20.000	-20.000	-25.000	-18.0	6.0
O	11.772	-5.330	-5.330	-5.787	-8.8	3.5
OB	11.694	-5.330	-5.330	-5.787	-8.8	3.5
OC	12.003	-10.000	-10.000	-12.000	-9.4	6.0
OH1	15.528	-5.920	-5.920	-9.264	-11.2	3.5
OS	6.774	-2.900	-2.900	-3.150	-4.8	3.5
S	20.703	-3.240	-3.240	-4.475	-39.9	3.5
SM	21.306	-3.240	-3.240	-4.475	-39.9	3.5

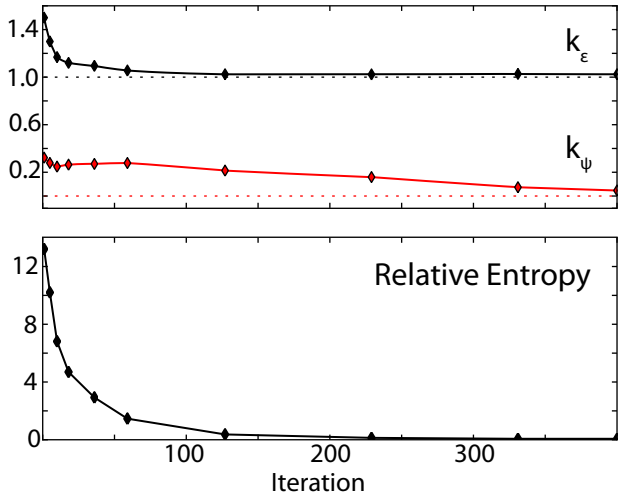

Figure 1: Validation of the relative entropy approach. We validate the relative entropy procedure by performing a reference molecular dynamics simulations on the $(\mathrm{AAQAA})_3$ peptide using the unoptimized EEF1-SB parameters. Then, we arbitrarily modified the values of k_ϵ and k_Ψ and performed a relative entropy minimization. Upper panel: convergence behaviour of the two parameters k_ϵ and k_Ψ (solid lines). At the end of the minimization, the parameters used in a reference simulation (dotted lines) are correctly recovered. The relative entropy calculated at each step of the procedure is shown in the bottom panel. Each sampling step (shown with points) is followed by a number of reweighting steps, where the relative entropy and the parameter update are estimated using perturbation techniques (see text).

Table 2: Partial atomic charges for ionic groups in EEF1-SB

Residue	Atom	Charge	Residue	Atom	Charge
ARG	CD	-0.30	HSP	CB	-0.10
	HD1/HD2	0.05		HB1/HB2	0.05
	NE	-0.28		CD2	0.05
	HE	0.12		HD2	0.00
	CZ	-0.20		CG	0.05
	NH1/NH2	-0.121		NE2/ND1	-0.55
	HH1/HH2	0.2005		HE2/HD1	0.45
				CE1	0.10
ASP	CB	-0.28		HE1	0.00
	HB1/HB2	0.14			
	HB1/HB2	0.14	LYS	CE	0.00
	HB1/HB2	0.14		HE1/HE2	0.00
				NZ	-0.90
GLU	CG	-0.28		HZ1/HZ2/HZ3	0.30
	HG1/HG2	0.14			
	CD	1.00			
	OE1/OE2	-0.50	NTER	N	-0.90
				HT1/HT2/HT3	0.20
GLP	CG	-0.21		HA	0.10
	HG1/HG2	0.09		CA	0.20
	CD	0.75			
	OE1	-0.55	CTER	C	1.00
	OE2	-0.61		OT1/OT2	-0.50
	HE2	0.44			

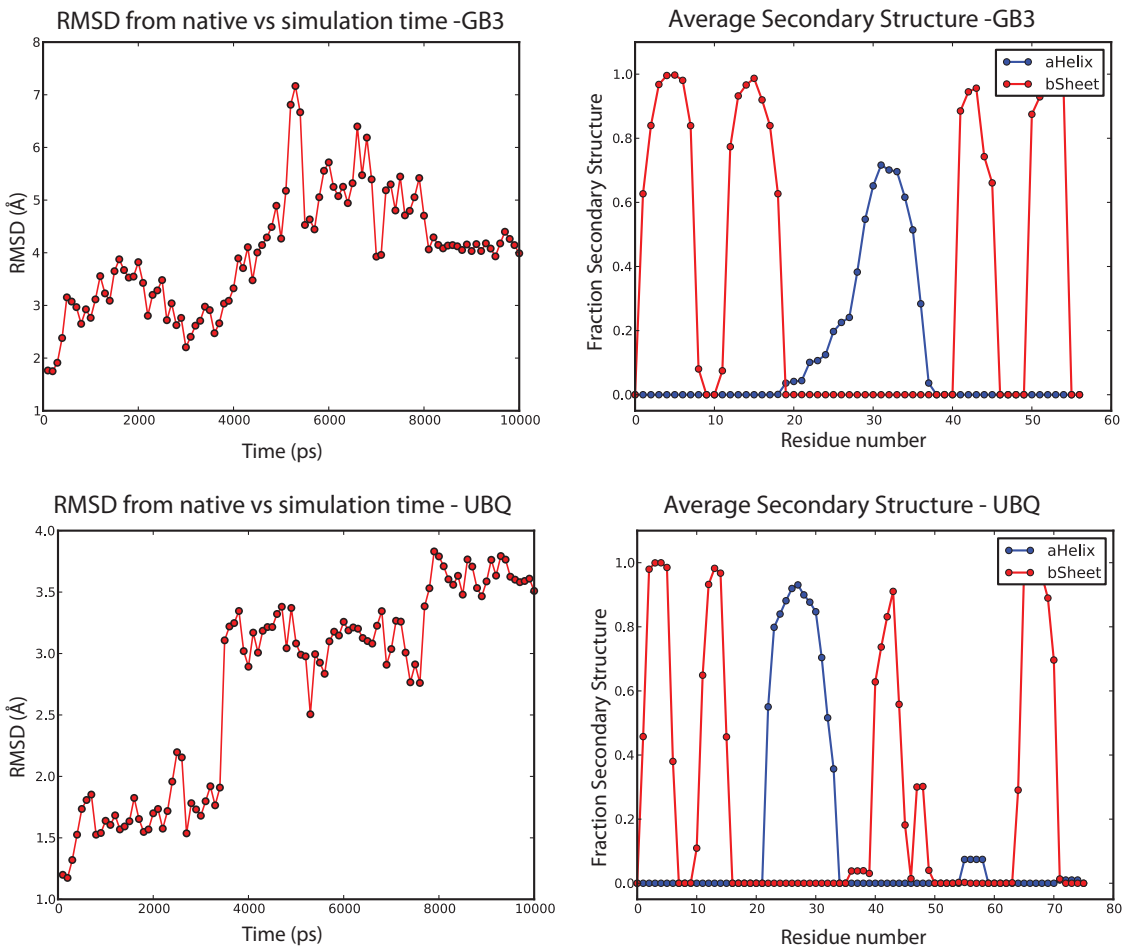

Figure 2: RMSD from native vs simulation time and average secondary structure content of GB3 and Ubiquitin using EEF1-SB.

Table 3: J-couplings for 19-residue peptide derived from hen lysozyme (HEWL19). The table gives the scalar couplings measured experimentally and calculated from the 298 K replica of REMD simulations using the "DFT2" Karplus relation, as described in the main text.

Residue/J	J_{expt}	J (C36/explicit)	J (EEF1-unopt.)	J (EEF1-SB)	J (FACTS)	J (SCPISM)
A9 $^{1}J_{\mathrm{NC}\alpha}$	10.54	10.40	9.88	10.80	9.75	9.79
A10 $^{1}J_{\mathrm{NC}\alpha}$	10.58	10.35	9.60	10.53	9.52	9.81
A11 $^{1}J_{\mathrm{NC}\alpha}$	10.57	10.40	10.23	10.65	9.73	9.80
A10 $^{2}J_{\mathrm{NC}\alpha}$	7.24	7.02	6.51	7.25	6.29	6.30
A11 $^{2}J_{\mathrm{NC}\alpha}$	7.02	6.91	7.20	6.76	6.74	6.24
A12 $^{2}J_{\mathrm{NC}\alpha}$	7.17	7.06	5.87	6.95	6.33	6.25
A9 $^{3}J_{\mathrm{H}\alpha\mathrm{C}}$	2.06	1.93	3.14	2.62	1.08	1.18
A10 $^{3}J_{\mathrm{H}\alpha\mathrm{C}}$	1.72	2.10	6.33	2.50	0.53	1.27
A11 $^{3}J_{\mathrm{H}\alpha\mathrm{C}}$	2.20	2.32	2.95	2.59	0.90	1.26
A9 $^{3}J_{\mathrm{HNC}}$	1.39	1.03	1.11	1.38	0.63	0.63
A10 $^{3}J_{\mathrm{HNC}}$	1.33	0.88	1.10	0.88	1.86	0.55
A11 $^{3}J_{\mathrm{HNC}}$	1.09	0.97	0.31	0.93	0.91	0.58
A9 $^{3}J_{\mathrm{HNC}\beta}$	2.26	2.77	0.57	1.34	3.83	3.72
A10 $^{3}J_{\mathrm{HNC}\beta}$	2.19	2.86	2.09	1.80	3.81	3.69
A11 $^{3}J_{\mathrm{HNC}\beta}$	2.21	2.73	1.61	1.57	3.88	3.69
A9 $^{3}J_{\mathrm{HNH}\alpha}$	5.18	6.15	10.26	7.90	4.88	5.11
A10 $^{3}J_{\mathrm{HNH}\alpha}$	5.10	6.19	6.15	8.13	2.55	5.34
A11 $^{3}J_{\mathrm{HNH}\alpha}$	5.67	6.23	9.85	8.47	4.22	5.29
A10 $^{3}J_{\mathrm{HNH}\alpha}$	0.46	0.37	0.37	0.53	0.10	0.16
A11 $^{3}J_{\mathrm{HNH}\alpha}$	0.43	0.38	0.34	0.49	0.10	0.16
A12 $^{3}J_{\mathrm{HNH}\alpha}$	0.43	0.41	0.48	0.54	0.12	0.16