Correction to Optimization of Protein Backbone Dihedral Angles by Means of Hamiltonian Reweighting

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The original manuscript described a Hamiltonian reweighting method to quickly scan a large number of force field parameters for peptide backbone dihedral angles, based on a single extensive simulation with a given force field. Parameter sets that lead to simulations with a close match to experimental data can be easily screened for. The method was applied on the GROMOS force field, parameter sets 54A7 and 54A8,[1,2] searching for dihedral angle parameters that better reproduce the ^{3}J-values and secondary structure propensities of all capped amino acids.[3,4]

To our embarrassment, we now realized that for a large portion of these mini-peptides the first peptide bond was in a cis conformation, rather than in the biologically more relevant trans conformation; see Figure 1. As the barrier for cis−trans

Figure 1. Graphical representation of the two backbone dihedral angles in the model systems. The angles ϕ and ψ are defined by atoms C−N−Cα−C and N−Cα−C−N, respectively. In accordance with the experimental studies, the amino acids are blocked: an acetyl group at the N-terminus and a *N*-methyl moiety at the C-terminus are used to ensure neutral ends. In the original article, a number of peptides were simulated with the first peptide bond in cis-configuration (A). The biologically most relevant configuration is the trans-configuration (B).

isomerization is rather high in the GROMOS force fields (67.0 kJ/mol), no transitions to the trans conformation were observed. While technically correct for a cis peptide, the original simulations and the optimized parameters do not correspond to biologically relevant configurations of the amino acids.

We have repeated the simulations of the capped amino acids as well as the screening for more optimal parameters and here report the most important data for the complete set of biologically relevant mini-peptides. Table 1 compares the parameters used in the 45A3, 53A6, 54A7, and 54A8 parameter sets to the reoptimized parameters for various subgroups (glycine, alanine, common amino acids, C$_\beta$-branched amino acids); it replaces Table 1 of the original manuscript. Figure 2 shows the potential energy profiles resulting from these parameters; it replaces Figure 5 of the original manuscript. Table 2 contains the J-values and helical propensities of the repeated simulations with the 54A8 parameter set, as well as the corresponding values obtained with various alternative parameter sets; it replaces Table 3 of the

original manuscript. Apart from the parameters in Table 1, Table 2 refers to individually optimized sets of parameters, which are described in Table 3. Table 3 replaces Table S5 of the original manuscript.

We apologize for any inconvenience the data for the cis peptides may have caused and emphasize that the methodological aspects of the manuscript remain unaltered. With the data provided in this correction, the optimized set of parameters can also be used in future simulations. Further optimizations are the subject of ongoing research.

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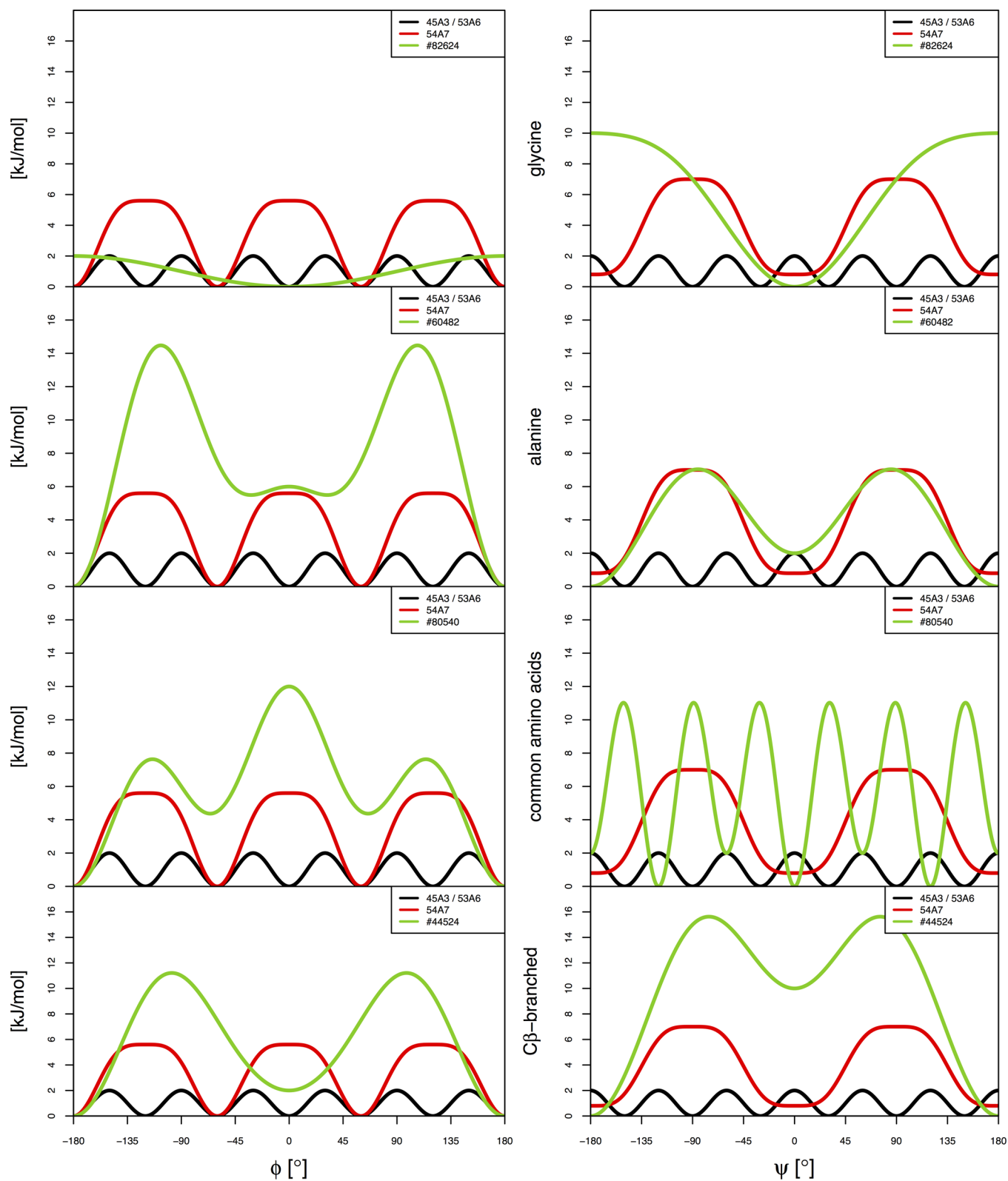## ■ ACKNOWLEDGMENTS

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Figure 2. Potential energy terms of Table 1. The top row represents the suggested parameters for glycine, the second row, those for alanine, the third row, those for the common amino acids subset, and the last row, those for the Cβ-branched amino acids, respectively. The left column shows the ϕ angle, and the right column, the ψ angle.

Table 1. Backbone Parameters of the GROMOS Force Field and Those of the Suggested Sets[a]

| | backbone angle potential energy functions | | | | | | |
| | ϕ | | | ψ | | | |
combination	K [kJ/mol]	shift [deg]	mult	K [kJ/mol]	shift [deg]	mult	description
45A3[b]/53A6[b]	1.0	180	6	1.0	0	6	refs 5 and 6
54A7/54A8	2.8	0	3	3.5	180	2	refs 1 and 2
	0.7	180	6	0.4	0	6	
#82624	1.0	180	1	1.0	180	2	glycine
	0.0	0	1	5.0	180	1	
#60482	5.0	180	2	3.0	180	2	alanine
	3.0	0	3	1.0	0	1	
#80540	3.0	0	3	5.0	180	6	common
	3.0	0	1	1.0	180	3	
#44524	5.0	180	2	5.0	180	2	C_β-branched
	1.0	0	3	5.0	0	1	

[a]All other combinations are provided in Table 3. [b]For these parameter sets, only one potential energy term is used to describe the ϕ and ψ backbone dihedral angles.

Table 2. Detailed Results of the Predicted and Simulated Parameter Combinations[a]

| | | J-value [Hz] | | propensities [%/100] | | | | | | Δ[b] | |
				P_α		P_β		P_{pII}		abs	ren
GLY	54A8[c]	5.5	(−0.4)	0.032	(−0.628)	0.129	(0.009)	0.192	(−0.028)	1.015	1.489
	#82624	5.9	(0.0)	0.162	(−0.498)	0.033	(−0.087)	0.047	(−0.173)	0.797	0.093
	#80540	5.1	(−0.8)	0.019	(−0.641)	0.151	(0.031)	0.085	(−0.135)	1.570	1.932
ALA	54A8[c]	6.2	(0.1)	0.107	(−0.003)	0.206	(−0.394)	0.603	(0.313)	0.829	0.869
	#60482	6.1	(0.0)	0.047	(−0.063)	0.606	(0.006)	0.209	(−0.081)	0.153	0.209
	#80540	6.8	(0.7)	0.046	(−0.064)	0.407	(−0.193)	0.461	(0.171)	1.171	1.172
ARG[d]	54A8[c]	6.5	(−0.4)	0.146	(0.076)	0.174	(−0.366)	0.570	(0.180)	0.982	1.049
	#80540	7.2	(0.3)	0.060	(−0.010)	0.357	(−0.183)	0.507	(0.117)	0.622	0.629
	#29753	6.8	(0.0)	0.068	(−0.002)	0.409	(−0.131)	0.448	(0.058)	0.194	0.198
ASN	54A8[c]	6.4	(−1.0)	0.113	(0.093)	0.206	(−0.374)	0.598	(0.198)	1.695	1.741
	#80540	7.1	(−0.4)	0.042	(0.022)	0.401	(−0.179)	0.495	(0.095)	0.681	0.690
	#65383	7.4	(0.0)	0.017	(−0.003)	0.524	(−0.056)	0.400	(0.000)	0.064	0.054
ASP[d]	54A8[c]	6.1	(−0.8)	0.096	(0.046)	0.183	(−0.277)	0.627	(0.137)	1.290	1.346
	#80540	6.7	(−0.2)	0.035	(−0.015)	0.385	(−0.075)	0.505	(0.015)	0.305	0.312
	#293	6.9	(0.0)	0.000	(−0.050)	0.457	(−0.003)	0.484	(−0.006)	0.061	0.102
CYS	54A8[c]	6.4	(−1.0)	0.131	(0.101)	0.234	(−0.306)	0.539	(0.109)	1.476	1.522
	#80540	7.0	(−0.3)	0.037	(0.007)	0.469	(−0.071)	0.406	(−0.024)	0.420	0.370
	#98338	7.3	(0.0)	0.016	(−0.014)	0.531	(−0.009)	0.421	(−0.009)	0.038	0.034
GLU[d]	54A8[c]	6.1	(−0.6)	0.095	(0.045)	0.130	(−0.230)	0.687	(0.097)	0.922	0.985
	#80540	6.8	(0.1)	0.042	(−0.008)	0.278	(−0.082)	0.616	(0.026)	0.247	0.267
	#88393	6.6	(0.0)	0.049	(−0.001)	0.332	(−0.028)	0.580	(−0.010)	0.058	0.047
GLN	54A8[c]	6.4	(−0.8)	0.124	(0.044)	0.161	(−0.319)	0.625	(0.185)	1.338	1.395
	#80540	7.0	(−0.1)	0.049	(−0.031)	0.341	(−0.139)	0.549	(0.109)	0.418	0.428
	#97635	7.1	(0.0)	0.013	(−0.067)	0.474	(−0.006)	0.449	(0.009)	0.083	0.132
HIS[d]	54A8[c]	6.8	(−1.1)	0.111	(0.071)	0.256	(−0.324)	0.533	(0.153)	1.658	1.701
	#80540	7.3	(−0.5)	0.040	(0.000)	0.453	(−0.127)	0.437	(0.057)	0.734	0.736
	#94540	7.9	(0.0)	0.030	(−0.010)	0.574	(−0.006)	0.343	(−0.037)	0.057	0.056
ILE	54A8[c]	6.3	(−1.0)	0.122	(0.102)	0.156	(−0.364)	0.669	(0.209)	1.715	1.750
	#44524	7.3	(0.0)	0.004	(−0.016)	0.552	(0.032)	0.385	(−0.075)	0.152	0.162
	#80540	7.1	(−0.2)	0.034	(0.014)	0.291	(−0.229)	0.645	(0.185)	0.659	0.671
	#28191	7.4	(0.0)	0.014	(−0.006)	0.530	(0.010)	0.447	(−0.013)	0.052	0.053
LEU	54A8[c]	6.3	(−0.6)	0.129	(0.029)	0.119	(−0.231)	0.671	(0.121)	0.962	1.022
	#80540	6.9	(0.1)	0.051	(−0.049)	0.280	(−0.070)	0.617	(0.067)	0.243	0.259
	#88384	6.9	(0.0)	0.072	(−0.028)	0.345	(−0.005)	0.540	(−0.010)	0.044	0.051
LYS[d]	54A8[c]	6.5	(−0.4)	0.136	(0.096)	0.169	(−0.241)	0.593	(0.043)	0.751	0.814
	#80540	7.1	(0.3)	0.056	(0.016)	0.348	(−0.062)	0.526	(−0.024)	0.393	0.362
	#21615	6.8	(0.0)	0.002	(−0.038)	0.404	(−0.006)	0.535	(−0.015)	0.065	0.080
MET	54A8[c]	6.5	(−0.5)	0.114	(0.084)	0.184	(−0.286)	0.604	(0.104)	0.994	1.052
	#80540	7.1	(0.1)	0.042	(0.012)	0.365	(−0.105)	0.525	(0.025)	0.268	0.282
	#64505	7.0	(0.0)	0.006	(−0.024)	0.431	(−0.039)	0.497	(−0.003)	0.071	0.070

Table 2. continued

		J-value [Hz]		propensities [%/100] P_α		P_β		P_{pII}		Δ^b abs	ren
PHE	54A8^c	6.7	(−0.4)	0.106	(0.046)	0.257	(−0.233)	0.547	(0.097)	0.826	0.865
	#80540	7.2	(0.1)	0.045	(−0.015)	0.441	(−0.049)	0.453	(0.003)	0.130	0.128
	#64469	7.2	(0.0)	0.021	(−0.039)	0.459	(−0.031)	0.440	(−0.010)	0.085	0.080
PRO	54A8^c	5.4	(0.0)	0.242	(0.002)	0.000	(0.000)	0.737	(−0.003)	0.006	0.020
	#80540	5.6	(0.2)	0.117	(−0.123)	0.001	(0.001)	0.848	(0.108)	0.421	0.447
SER	54A8^c	6.4	(−0.7)	0.151	(0.111)	0.238	(−0.232)	0.496	(0.006)	1.019	1.073
	#80540	6.9	(−0.1)	0.041	(0.001)	0.490	(0.020)	0.370	(−0.120)	0.248	0.265
	#48221	7.0	(0.0)	0.009	(−0.031)	0.455	(−0.015)	0.459	(−0.031)	0.083	0.066
THR	54A8^c	6.3	(−1.1)	0.397	(0.367)	0.092	(−0.488)	0.452	(0.062)	2.008	2.055
	#44524	7.4	(0.1)	0.018	(−0.012)	0.562	(−0.018)	0.373	(−0.017)	0.118	0.092
	#80540	8.0	(0.6)	0.172	(0.142)	0.337	(−0.243)	0.345	(−0.045)	1.033	0.975
	#65713	7.4	(0.0)	0.020	(−0.010)	0.569	(−0.011)	0.363	(−0.027)	0.053	0.041
TRP	54A8^c	6.4	(−0.5)	0.103	(0.083)	0.223	(−0.217)	0.608	(0.068)	0.867	0.902
	#80540	8.1	(1.2)	0.047	(0.027)	0.504	(0.064)	0.347	(−0.193)	1.453	1.476
	#91948	6.9	(0.0)	0.011	(−0.009)	0.429	(−0.011)	0.539	(−0.001)	0.047	0.047
TYR	54A8^c	6.8	(−0.3)	0.100	(0.030)	0.275	(−0.195)	0.533	(0.073)	0.618	0.654
	#80540	8.4	(1.2)	0.039	(−0.031)	0.553	(0.083)	0.285	(−0.175)	1.513	1.546
	#96433	7.1	(0.0)	0.060	(−0.010)	0.447	(−0.023)	0.436	(−0.024)	0.074	0.030
VAL	54A8^c	6.3	(−1.1)	0.133	(0.113)	0.147	(−0.363)	0.669	(0.199)	1.725	1.760
	#44524	7.3	(0.0)	0.004	(−0.016)	0.531	(0.021)	0.757	(0.287)	0.355	0.262
	#80540	8.1	(0.8)	0.038	(0.018)	0.443	(−0.067)	0.514	(0.044)	0.913	0.914
	#98311	7.3	(0.0)	0.019	(−0.001)	0.514	(0.004)	0.454	(−0.016)	0.031	0.032

^{a}Deviations with respect to the experimental target values are reported in parentheses. The combinations given in italics indicate the best hits when the amino acids were optimized individually and thus give the best hits possible with our screening set of parameters. ^{b}The overall Δ is the sum of the absolute values of the deviation of the J-value (Hz) and the discrepancies in the propensities (%/100) (see eq 4 of the original manuscript). The "abs" column refers to the deviation when the absolute occurrences of the three secondary structure classes were used, while the "ren" column refers to the average deviations when the propensities were first renormalized to 100%. ^{c}These values were computed from real simulations and were not projected. ^{d}In terms of protonation states, we used GROMOS parameters for HISA (neutral charge, protonated at N$_\delta$), LYSH (+1 charge), ARG (+1 charge), and the dissociated versions of glutamic acid (GLU) and aspartic acid (ASP).

Table 3. Parameter Combinations for the Individually Optimized Amino Acids

	torsional angle parameters						
	ϕ K [kJ/mol]	shift [deg]	mult	ψ K [kJ/mol]	shift [deg]	mult	description
#29753	5	0	3	5	180	2	arginine
	5	0	1	1	0	1	
#65383	5	180	6	3	180	3	asparagine
	1	180	1	1	0	1	
#293	3	0	3	5	0	1	aspartate
	3	0	1	5	0	1	
#98338	5	180	6	5	180	6	cysteine
	1	180	1	5	180	3	
#88393	3	180	6	5	180	3	glutamate
	1	0	3	3	180	2	
#97635	3	180	2	5	180	3	glutamine
	1	180	1	1	180	3	
#94540	3	180	6	5	180	3	histidine
	1	180	1	1	180	1	
#98338	5	180	6	5	180	6	isoleucine
	1	180	1	5	180	3	
#88384	3	180	6	3	180	3	leucine
	1	0	3	3	180	2	
#21615	5	180	6	5	0	1	lysine
	3	180	1	3	0	1	
#64505	5	180	6	3	180	2	methionine
	3	180	1	5	0	1	
#64469	5	180	6	1	180	2	phenylalanine
	3	180	1	3	0	1	
#48221	3	180	6	3	180	6	serine

Table 3. continued

| | torsional angle parameters | | | | | | |
| | ϕ | | | ψ | | | description |
	K [kJ/mol]	shift [deg]	mult	K [kJ/mol]	shift [deg]	mult	
	1	0	3	5	0	1	
#65713	5	180	6	5	180	3	threonine
	5	180	2	3	0	1	
#91948	3	180	6	5	180	6	tryptophan
	1	0	3	5	180	3	
#96433	5	180	6	3	180	3	tyrosine
	3	180	1	3	180	2	
#98311	5	180	6	5	180	6	valine
	1	180	1	3	180	3	