Supplemental Material

Interactions of Amino Acid Side Chain Analogs within Membrane Environments

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Tables

Table S1: Simulation time in nanoseconds for explicit solvent simulations of amino-acid analog pairs at different umbrella potentials. Sampling in forward and backward directions (see text) were simulated for the same time.

	z	3	3.5	4	4.5	5	5.5	6	6.5	7	7.5	8	8.5	9	9.5	10	10.5	11	11.5	12	12.5	13	13.5	14	14.5	15
Acetamide	0	20	20	30	20	20	200	120	20	20	20	20	20	20	10	10	10	20	20	30	20	20	200	120	20	20
	4	30	70	30	50	200	90	150	50	50	30	30	20	20	10	10	10	30	70	30	50	200	90	150	50	50
	8	20	20	20	20	20	20	20	20	20	20	20	20	20	10	20	10	20	20	20	20	20	20	20	20	20
	12	20	20	20	20	20	20	20	20	20	20	20	20	20	10	10	10	20	20	20	20	20	20	20	20	20
	16	20	20	30	30	30	30	30	30	30	30	30	30	30	40	14	10	20	20	30	30	30	30	30	30	30
	20	20	20	20	20	20	20	20	20	20	20	20	20	20	10	10	10	20	20	20	20	20	20	20	20	20
	24	20	20	20	20	20	20	20	20	20	20	20	20	20	10	10	10	20	20	20	20	20	20	20	20	20
Methanol	0	20	20	20	20	20	20	20	20	50	20	20	20	20	10	10	10	20	20	20	20	20	20	20	20	50
	4	20	20	20	200	30	30	20	20	20	20	20	20	20	10	10	10	20	20	20	200	30	30	20	20	20
	8	20	20	92	40	20	20	20	20	20	30	20	30	20	10	10	10	20	20	92	40	20	20	20	20	20
	12	20	20	20	20	20	20	20	20	20	20	20	20	20	10	10	10	20	20	20	20	20	20	20	20	20
	16	20	20	50	20	20	20	20	20	20	20	20	20	20	10	10	10	20	20	50	20	20	20	20	20	20
	20	20	20	20	20	20	20	20	20	20	20	20	20	20	10	10	10	20	20	20	20	20	20	20	20	20
	24	20	20	20	20	20	20	20	20	20	20	20	20	20	10	10	10	20	20	20	20	20	20	20	20	20
Toluene	0	12	12	12	12	12	12	12	12	12	12	12	12	12	10	10	10	12	12	12	12	12	12	12	12	12
	4	12	12	12	20	12	12	12	12	12	12	12	12	12	10	10	10	12	12	12	20	12	12	12	12	12
	8	12	12	12	12	12	20	12	12	12	12	12	12	12	10	10	10	12	12	12	12	12	20	12	12	12
	12	12	12	12	12	40	40	40	40	20	20	30	20	20	10	62	10	12	12	12	12	40	40	40	40	20
	16	70	70	70	70	40	40	40	40	40	40	40	40	40	40	10	30	70	70	70	70	40	40	40	40	40
	20	12	12	12	12	12	12	20	12	12	12	12	12	12	10	10	10	12	12	12	12	12	12	20	12	12
	24	12	12	12	12	12	12	12	30	30	12	12	12	12	10	10	10	12	12	12	12	12	12	12	30	30
Propane	0	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	4	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	8	6	6	6	6	6	20	6	6	6	6	6	20	6	6	20	6	6	6	6	6	6	20	6	6	6
	12	6	6	16	16	16	16	16	16	30	30	30	16	30	30	20	6	6	6	16	16	16	16	16	16	30
	16	6	30	30	30	30	30	30	30	40	100	40	60	30	20	20	6	6	30	30	30	30	30	30	30	40
	20	6	6	6	6	6	6	6	6	20	20	6	6	6	6	20	20	6	6	6	6	6	6	6	6	20
	24	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6

Table S2: Improved HDGB parameters, dielectric profile (ε) and non-polar profile (γ)

z	ε(z) - old	ε(z) - new
0.0	1.80	1.15
0.5	1.80	1.15
1.0	1.81	1.16
1.5	1.82	1.17
2.0	1.83	1.18
2.5	1.84	1.19
3.0	1.85	1.20
3.5	1.86	1.21
4.0	1.87	1.22
4.5	1.89	1.24
5.0	1.91	1.26
5.5	1.93	1.28
6.0	1.97	1.32
6.5	2.00	1.35
7.0	2.04	1.49
7.5	2.09	1.64
8.0	2.15	1.80
8.5	2.22	1.87
9.0	2.31	1.96
9.5	2.41	2.06
10.0	2.53	2.18
10.5	3.23	2.28
11.0	3.63	2.38
11.5	4.13	2.58
12.0	4.73	2.89
12.5	5.43	3.42
13.0	6.13	4.00
13.5	6.98	5.08
14.0	7.84	6.04
14.5	8.80	7.50
15.0	10.96	10.06
15.5	14.05	13.75
16.0	19.04	19.04
16.5	25.85	25.85
17.0	35.38	35.38
17.5	45.88	45.88
18.0	54.11	54.11
18.5	60.79	60.79
19.0	65.52	65.52
19.5	69.42	69.42
20.0	72.31	72.31
20.5	74.07	74.07
21.0	75.53	75.53
21.5	76.63	76.63
22.0	77.14	77.14
22.5	77.83	77.83
23.0	78.22	78.22
23.5	78.92	78.92
24.0	79.35	79.35
24.5	79.66	79.66
25.0	80.00	80.00

z	γ(z)
0.0	0.0000
0.6	0.0001
1.2	0.0002
1.8	0.0010
2.4	0.0050
3.0	0.0075
3.6	0.0100
4.2	0.0150
4.8	0.0200
5.4	0.0250
6.0	0.0300
6.6	0.0350
7.2	0.0410
7.8	0.0470
8.4	0.0520
9.0	0.0610
9.6	0.0720
10.2	0.0850
10.8	0.1000
11.4	0.1200
12.0	0.1500
12.6	0.1900
13.2	0.2500
13.8	0.3200
14.4	0.4000
15.0	0.5000
15.6	0.6200
16.2	0.7500
16.8	0.8753
17.4	0.9500
18.0	1.0308
18.6	1.0680
19.2	1.0921
19.8	1.1000
20.4	1.1000
21.0	1.0927
21.6	1.0690
22.2	1.0468
22.8	1.0328
23.4	1.0197
24.0	1.0130
24.6	1.0052
25.2	1.0005
25.8	1
26.4	1
27.0	1
27.6	1
28.2	1
28.8	1
29.4	1
30.0	1

Figures

Figure S1: Amino acid analogs used in this study: acetamide (Asn), methanol (Ser), toluene (Phe) and propane (Val)

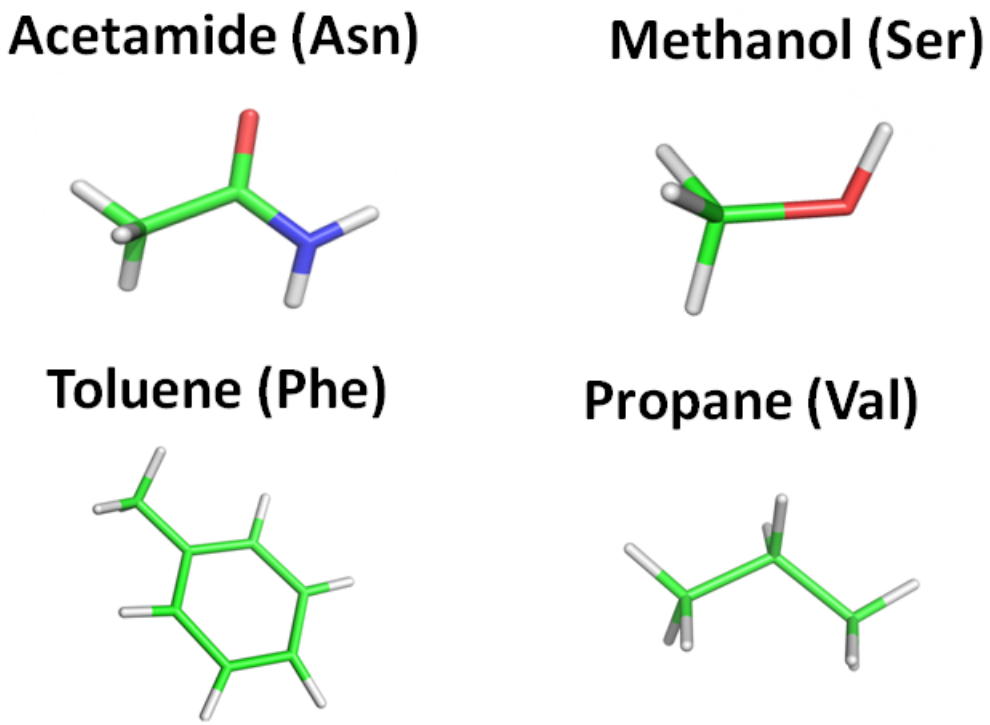


Figure S2: Root mean square deviation between the PMF profiles for each umbrella in forward and backward directions.

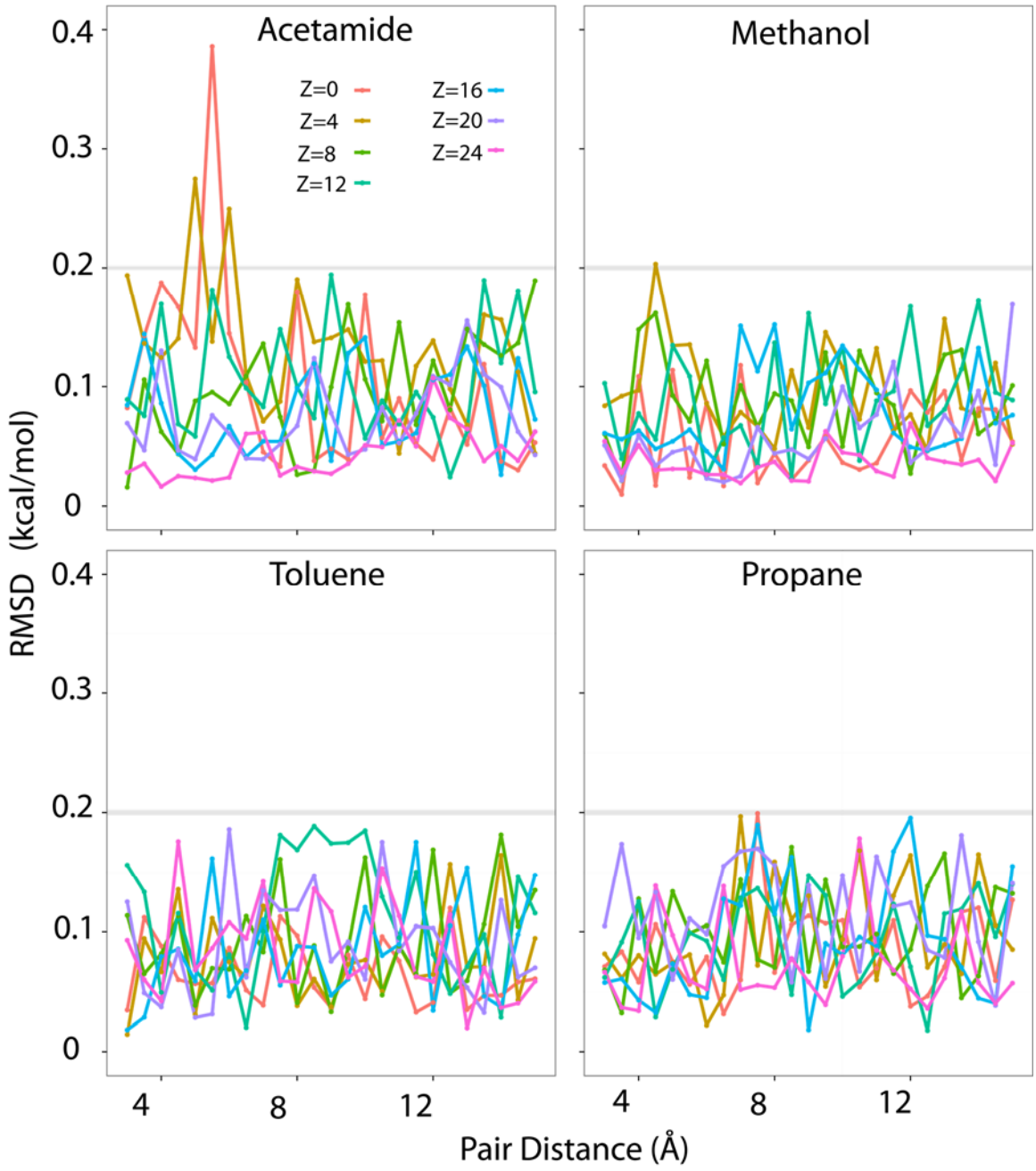


Figure S3. A: 2D PMF of acetamide pair association at z=0 and water density in biasing cylinder; B: Corrected 1D PMF as a function of pair distance after Boltzmann averaging along the water density reaction coordinate.

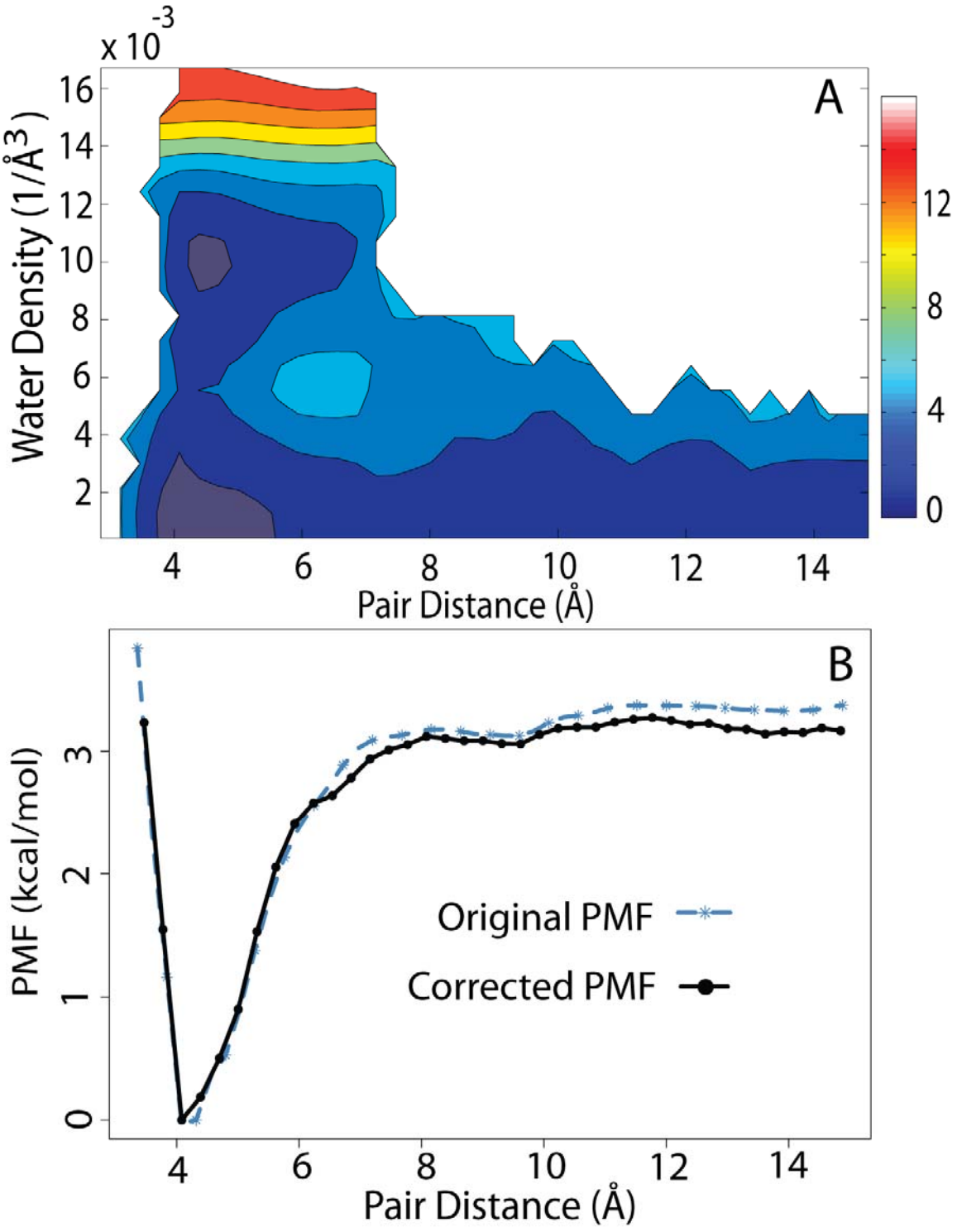


Figure S4. A: 2D PMF of methanol pair association at z=4 Å and water density in biasing cylinder; B: Corrected 1D PMF as a function of pair distance after Boltzmann averaging along the water density reaction coordinate.

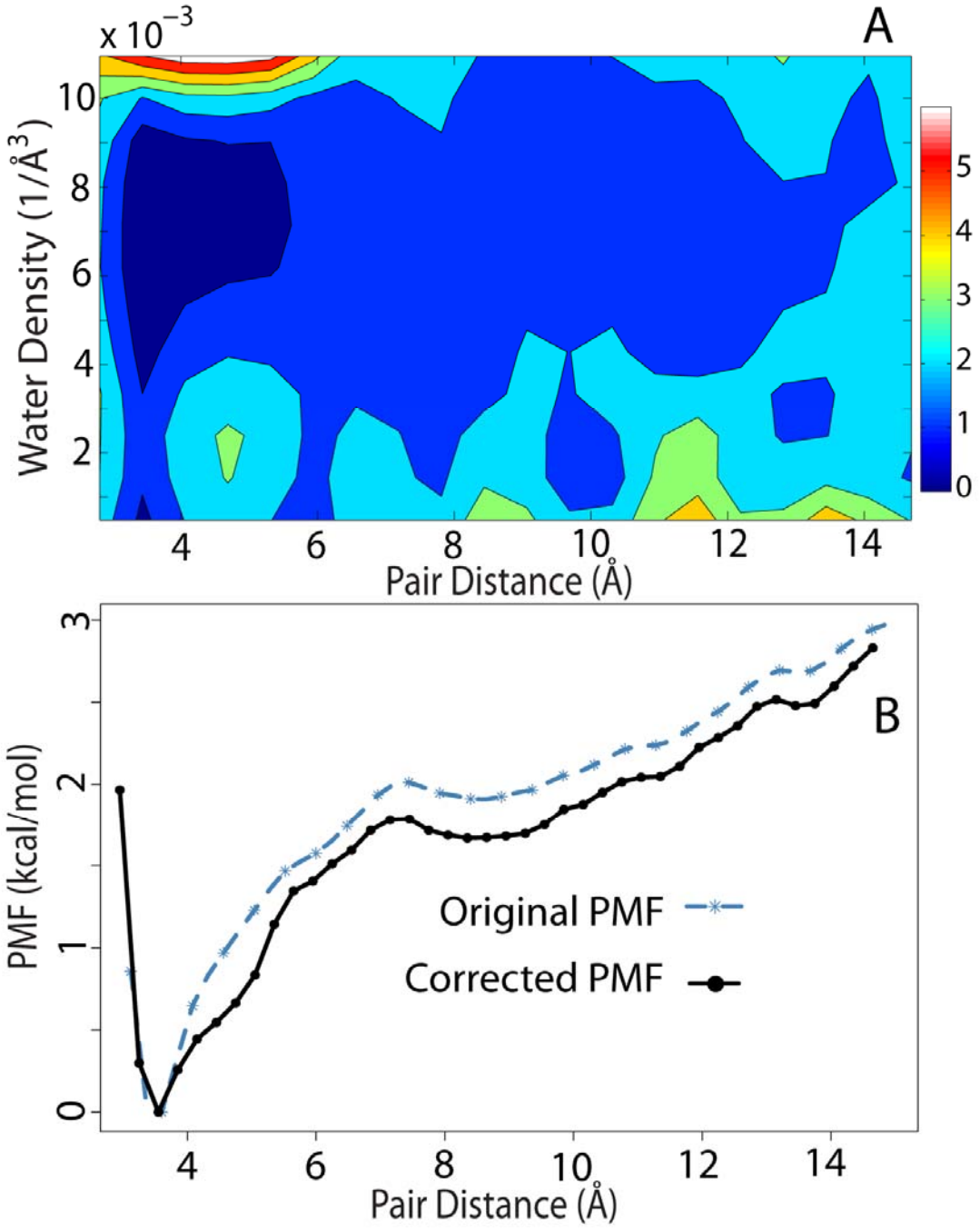
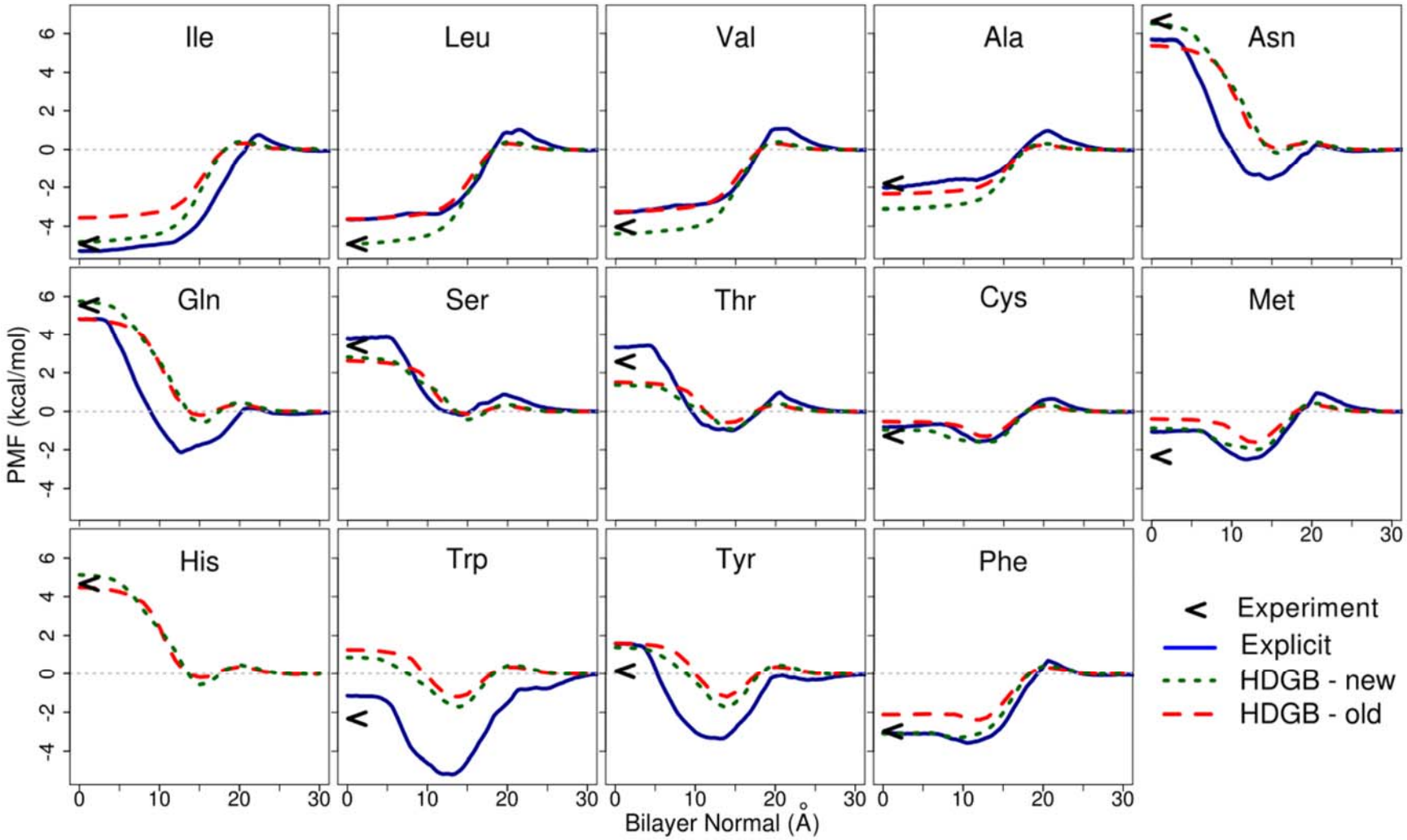


Figure S5: Free energy profiles of insertion of single amino acid side-chain analogs using HDGB simulations with old and improved parameters compared with results of explicit simulation[1] and experimental measurements[2]



1. MacCallum JL, Bennett WFD, Tieleman DP. Distribution of Amino Acids in a Lipid Bilayer from Computer Simulations. Biophys J 2008;94:3393-3404.
2. Radzicka A, Wolfenden R. Comparing the polarities of the amino acids: side-chain distribution coefficients between the vapor phase, cyclohexane, 1-octanol, and neutral aqueous solution. Biochemistry 1988;27:1664-1670.