Supporting Information for

Benchmarking of Force Fields for Molecule-Membrane Interactions

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***Table S1**: Duration of z-constraint simulations. All windows were calculated for 30 ns and when marked, specific slowly converging simulations were prolonged to 50 ns.*

Molecule	Simulation time (ns)				
	Berger	Slipids	CHARMM36	GAFFlipids	GROMOS 43A1-S3
glycerol	30	50	50	30	30
methanol	30	30	50	30	30
acetone	50	50	50	50	50
1-butanol	50	50	50	50	50
benzylalcohol	50	50	50	50	50
aniline	50	50	50	50	50
2-nitrotoluene	50	50	50	50	50
xylene	50	50	50	30	50
4-chloro-3-methylphenol	50	50	50	50	50
2,4,5-trichloroaniline	30	50	50	50	50
hexachlorobenzene	30	50	50	50	30

***Table S2**: Approximate CPU time required for computing 1 ns of the z-constraint simulation, for calculation of topology of each molecule (in the case of COSMOmic for DFT calculation of σ-profile) and the total CPU hours for the project (30 ns per simulation window of z-constraint simulation are considered here).*

Force Field	Constraint CPU hour/ns	CPU hours/topology	CPU hours/project
Berger	6.4	3	21200
Slipids	21.6	3	71300
CHARMM36	44.0 (30.4 by cut-off 1.2 nm)	- (ParamChem)	145200
GAFFlipids	13.6	0.1	44900
GROMOS 43A1-S3	10.4	3	34400
COSMOmic	-	0.1	3

***Table S3**: Logarithms of partition coefficients between DMPC membrane and water (Log K) measured experimentally (Exp.) and calculated by considered FFs and COSMOmic. The mean differences, mean absolute differences and Spearman`s rank order correlation coefficient are calculated with respect to experiment.*

Molecule	Log K						
	Exp.	Berger	Slipids	CHARMM36	GAFFlipids	GROMOS 43A1-S3	COSMOmic
glycerol	-1.04	-0.07	0.23	-2.10	0.50	-0.30	0.24
methanol	-0.53	-0.31	-0.57	-1.72	-0.47	-0.37	0.00
acetone	0.06	0.69	0.04	-0.61	-3.00	0.42	0.37
1-butanol	0.51	1.34	1.39	1.32	2.07	-0.15	1.31
benzylalcohol	1.14	4.11	1.11	1.29	1.12	0.65	1.66
aniline	1.63	2.56	1.13	0.90	1.65	0.39	1.71
2-nitrotoluene	2.41	6.25	1.64	2.56	2.46	6.50	3.16
xylene	2.98	3.34	3.12	2.03	2.90	1.82	3.87
4-chloro-3-methylphenol	3.34	3.71	3.60	2.64	4.17	2.41	2.78
2,4,5-trichloroaniline	4.16	5.58	4.43	4.28	3.74	2.96	3.33
hexachlorobenzene	5.64	10.06	6.08	4.99	5.19	4.75	5.34
Statistics							
Mean difference		1.54	0.17	-0.43	0.00 (0.31)	-0.11 (-0.53)	0.32
Mean absolute difference		1.54	0.42	0.65	0.74 (0.50)	1.08 (0.78)	0.62
Spearman`s rank order correlation coefficient		0.86	0.96	0.96	0.93	0.85	0.95

***Table S4**: Penetration barriers ΔG^{pen} calculated by considered FF and COSMOmic. The mean differences and mean absolute differences are calculated with respect to values from Slipids FF.*

Molecule	ΔG^{pen} (kcal/mol)					
	Berger	Slipids	CHARMM36	GAFFlipids	GROMOS 43A1-S3	COSMOmic
glycerol	6.58	5.81	6.92	6.04	9.14	5.03
methanol	5.05	3.09	3.53	3.46	2.11	3.57
acetone	1.80	1.22	1.31	9.38	0.91	0.90
1-butanol	4.73	1.66	2.46	2.77	3.12	2.16
benzylalcohol	1.70	3.60	3.20	2.56	2.60	2.12
aniline	2.30	3.03	2.84	2.47	2.43	1.93
2-nitrotoluene	2.23	2.03	1.12	2.26	1.08	1.99
xylene	0.00	0.00	0.94	0.29	0.34	0.03
4-chloro-3-methylphenol	2.31	2.90	1.00	4.66	0.58	0.72
2,4,5-trichloroaniline	1.51	3.18	0.90	3.59	0.58	0.24
hexachlorobenzene	0.00	0.17	0.85	0.68	0.00	0.00
Statistics						
Mean difference	0.14		-0.15	1.04 (0.33)	-0.35 (-0.29)	-0.73
Mean absolute difference	1.06		0.89	1.33 (0.65)	1.28 (1.31)	0.91

Table S5: *Water/lipids barriers ΔG^{wat} calculated by all FF and COSMOmic. The mean differences and mean absolute differences are calculated with respect to values from Slipids FF.*

Molecule	ΔG^{wat} (kcal/mol)					
	Berger	Slipids	CHARMM36	GAFFlipids	GROMOS 43A1-S3	COSMOmic
glycerol	0.42	0.77	0.04	1.10	0.67	0.93
methanol	0.25	0.09	0.10	0.40	0.34	0.73
acetone	1.58	1.09	0.00	0.00	1.08	0.92
1-butanol	2.54	3.02	2.71	3.57	0.91	2.62
benzylalcohol	6.65	2.24	2.47	2.23	1.76	3.11
aniline	4.32	2.19	1.91	3.03	1.02	3.24
2-nitrotoluene	9.54	2.94	4.43	4.16	9.89	4.89
xylene	5.16	4.95	5.70	4.29	3.02	5.92
4-chloro-3-methylphenol	5.79	5.54	4.33	6.38	4.02	4.50
2,4,5-trichloroaniline	8.72	6.96	6.65	5.90	4.78	4.89
hexachlorobenzene	14.95	8.73	7.20	7.72	7.26	8.05
Statistics						
Mean difference	1.94		-0.27	0.02 (0.14)	-0.34 (-1.07)	0.12
Mean absolute difference	2.09		0.72	0.72 (0.68)	1.65 (1.12)	0.91

***Table S6**: Positions of free energy minima calculated by all FF and COSMOmic. The mean differences and mean absolute differences are calculated with respect to values from Slipids.*

Molecule	Position of free energy minimum (nm)					
	Berger	Slipids	CHARMM36	GAFFlipids	GROMOS 43A1-S3	COSMOmic
glycerol	1.80	1.30	2.89	1.40	2.40	2.11
methanol	1.21	2.51	2.71	1.30	2.11	1.90
acetone	1.19	0.99	3.10	3.19	0.89	1.90
1-butanol	0.89	0.99	1.01	1.10	1.98	1.11
benzylalcohol	0.91	1.00	1.01	1.11	0.89	1.11
aniline	1.19	1.20	1.01	1.29	1.80	1.11
2-nitrotoluene	0.91	1.00	0.81	1.30	0.90	0.89
xylene	0.00	0.01	1.00	0.71	0.61	0.75
4-chloro-3-methylphenol	1.20	1.00	1.00	1.11	0.59	1.04
2,4,5-trichloroaniline	0.90	1.00	0.90	1.10	0.58	1.04
hexachlorobenzene	0.00	0.49	0.71	0.80	0.00	0.00
Statistics						
Mean difference	-0.12		0.42	0.26 (0.07)	0.11 (0.14)	0.13
Mean absolute difference	0.28		0.51	0.49 (0.31)	0.48 (0.52)	0.37

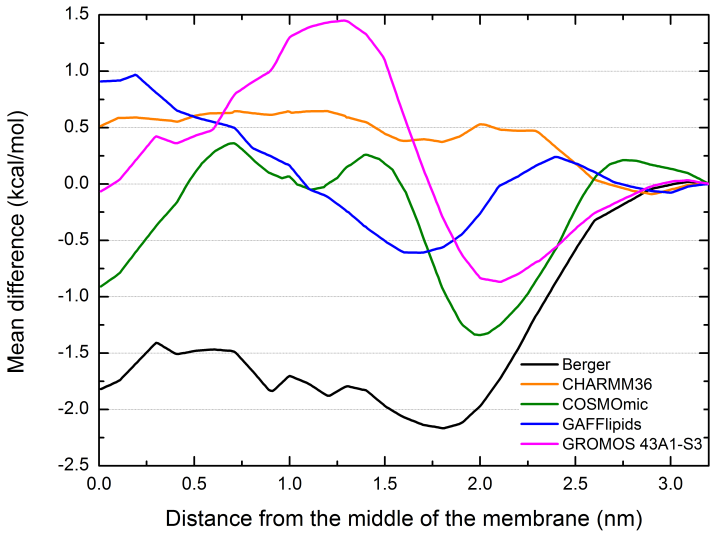

Figure S1: Mean difference of free energy values in various membrane depths in respect to free energy calculated in Slipids force field shows regions with increased (below zero) and reduced (above zero) affinity to that region.