An Analysis of Biomolecular Force Fields for Simulations of Polyglutamine in Solution (Supplementary Information)

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Abstract

This document contains supplementary material.

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SIMULATION DETAILS

Force field(s)	Replica temperatures (K)
AMBER ff99	298.00; 300.31; 302.63; 304.96; 307.31; 309.67; 312.05; 314.43; 316.84; 319.25; 321.68; 324.12; 326.58; 329.05; 331.54; 333.79; 336.30; 338.82; 341.37; 343.92; 346.49; 349.08; 351.68; 354.30; 356.93; 359.58; 362.24; 364.91; 367.61; 370.31; 373.04; 375.78; 378.54; 381.31; 384.09; 386.90; 389.72; 392.56; 395.41; 398.28; 401.17; 404.08; 406.99; 409.93; 412.89; 415.86; 418.85; 421.86; 424.89; 427.93; 430.96; 434.04; 437.14; 440.26; 443.39; 446.55; 449.71; 452.90; 456.11; 459.34
GROMOS96 53a6, GROMOS96 54a7	298.00; 299.88; 301.77; 303.67; 305.58; 307.50; 309.43; 311.40; 313.35; 315.30; 317.27; 319.25; 321.24; 323.23; 325.24; 327.26; 329.29; 331.33; 333.38; 335.44; 337.50; 339.58; 341.68; 343.78; 345.89; 348.02; 350.15; 352.30; 354.44; 356.60; 358.78; 360.97; 363.17; 365.38; 367.61; 369.85; 372.10; 374.35; 376.62; 378.90; 381.19; 383.50; 385.81; 388.13; 390.47; 392.83; 395.19; 397.57; 399.96; 402.36; 404.77; 407.20; 409.66; 412.11; 414.58; 417.05; 419.55; 422.05; 424.56; 427.09; 429.63; 432.18; 434.74; 437.32; 439.92; 442.52; 445.14; 447.78; 450.43; 453.09; 455.76; 458.58
All others	298.00; 300.08; 302.17; 304.28; 306.39; 308.52; 310.66; 312.81; 314.97; 317.14; 319.33; 321.52; 323.73; 325.96; 328.19; 330.43; 332.70; 334.97; 337.25; 339.54; 341.85; 344.18; 346.51; 348.86; 351.21; 353.58; 355.97; 358.36; 360.77; 363.20; 365.63; 368.09; 370.55; 373.03; 375.53; 378.04; 380.56; 383.09; 385.64; 388.20; 390.78; 393.37; 395.97; 398.59; 401.22; 403.87; 406.53; 409.21; 411.90; 414.61; 417.33; 420.07; 422.82; 425.59; 428.37; 431.17; 433.98; 436.81; 439.66; 442.52; 445.39; 448.29; 451.20; 454.12; 457.06; 460.02; 463.00; 465.99; 469.00; 472.02; 475.06; 478.12

Table S1: Replica temperatures in REMD simulation.

ESTIMATES OF SAMPLING ERROR

Estimates of the sampling error, where provided, were calculated by a block averaging approach. Each production MD simulation was 100 ns in length. For a given quantity (e.g. R_g), block averages of the quantity were computed over the first and

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second 50-ns halves of the simulation. The mean absolute deviation of the two block averages with respect to the total average was taken as the sampling error.

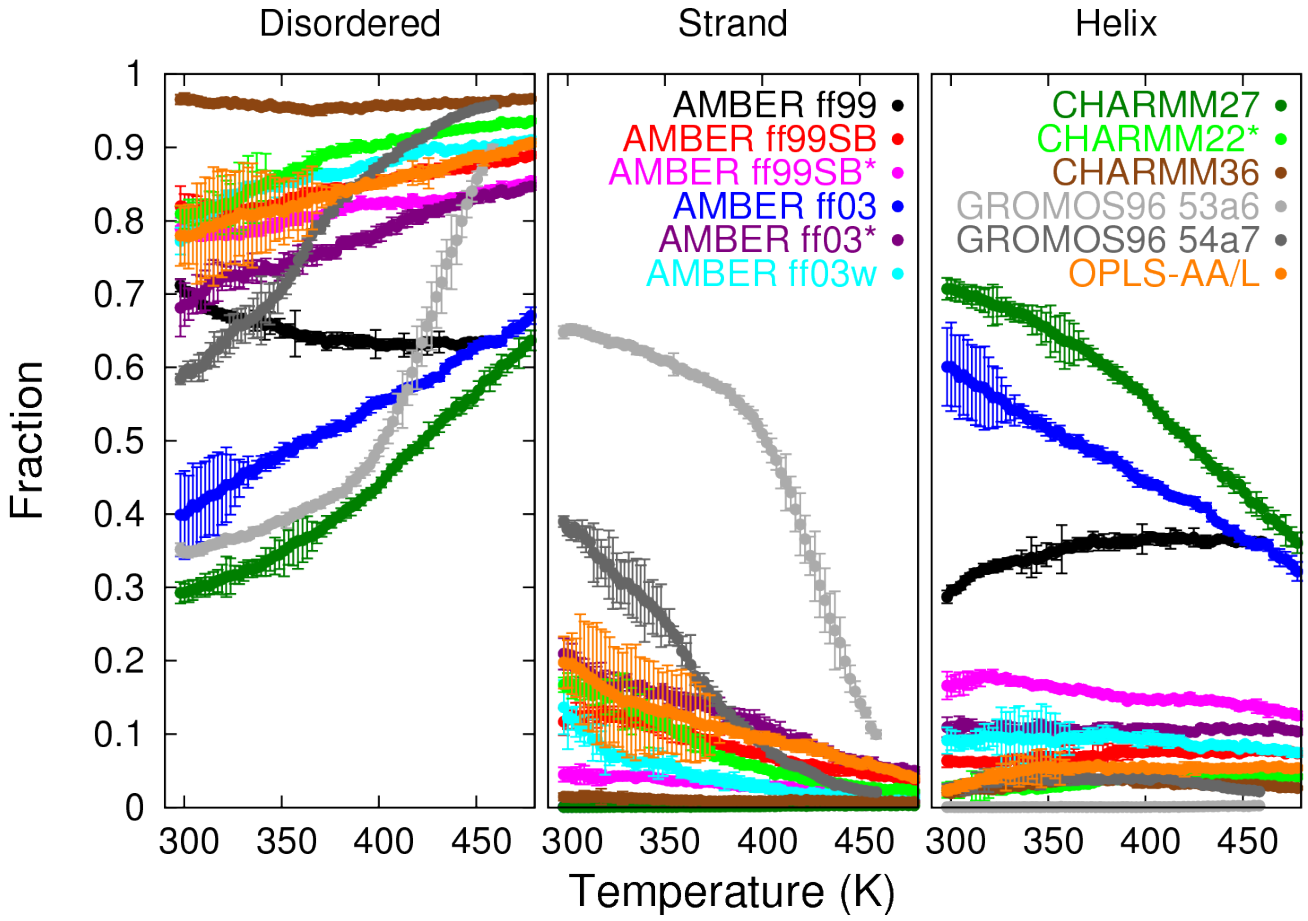

Figure S1: Average fractional secondary structure of Q_{30} in water. Left to right, the disordered (f_d), strand-like (f_s), and helix-like (f_h) fractions are plotted for all temperatures.

Force field	f_d	f_s	f_h
AMBER ff99	0.712 ± 0.009	0.001 ± 0.000	0.287 ± 0.009
AMBER ff99SB	0.820 ± 0.028	0.117 ± 0.019	0.063 ± 0.009
AMBER ff99SB*	0.789 ± 0.015	0.045 ± 0.010	0.166 ± 0.019
AMBER ff03	0.399 ± 0.056	0.000 ± 0.000	0.601 ± 0.053
AMBER ff03*	0.681 ± 0.039	0.209 ± 0.021	0.109 ± 0.014
AMBER ff03w	0.772 ± 0.018	0.136 ± 0.037	0.091 ± 0.018
CHARMM27	0.293 ± 0.015	0.000 ± 0.000	0.707 ± 0.015
CHARMM22*	0.809 ± 0.011	0.167 ± 0.010	0.023 ± 0.010
CHARMM36	0.965 ± 0.007	0.014 ± 0.005	0.020 ± 0.003
GROMOS96 53a6	0.352 ± 0.008	0.648 ± 0.008	0.000 ± 0.000
GROMOS96 54a7	0.584 ± 0.007	0.390 ± 0.007	0.026 ± 0.005
OPLS-AA/L	0.780 ± 0.041	0.198 ± 0.035	0.023 ± 0.006

Table S2: Fractional secondary structure of Q_{30} in water at 298 K.

Force field	Temperature (K)	f_d	f_s	f_h
AMBER ff99	459	0.634 ± 0.005	0.003 ± 0.001	0.363 ± 0.005
AMBER ff99SB	478	0.890 ± 0.004	0.037 ± 0.023	0.073 ± 0.004
AMBER ff99SB*	478	0.854 ± 0.005	0.020 ± 0.003	0.125 ± 0.006
AMBER ff03	478	0.670 ± 0.011	0.000 ± 0.000	0.322 ± 0.013
AMBER ff03*	478	0.847 ± 0.005	0.050 ± 0.005	0.103 ± 0.004
AMBER ff03w	478	0.910 ± 0.005	0.015 ± 0.003	0.075 ± 0.006
CHARMM27	478	0.637 ± 0.014	0.002 ± 0.000	0.361 ± 0.014
CHARMM22*	478	0.936 ± 0.013	0.022 ± 0.002	0.042 ± 0.003
CHARMM36	478	0.966 ± 0.002	0.007 ± 0.001	0.026 ± 0.002
GROMOS96 53a6	459	0.898 ± 0.006	0.010 ± 0.006	0.002 ± 0.001
GROMOS96 54a7	459	0.958 ± 0.002	0.021 ± 0.002	0.021 ± 0.002
OPLS-AA/L	478	0.906 ± 0.005	0.040 ± 0.003	0.054 ± 0.003

Table S3: Fractional secondary structure of Q_{30} in water at elevated temperatures.

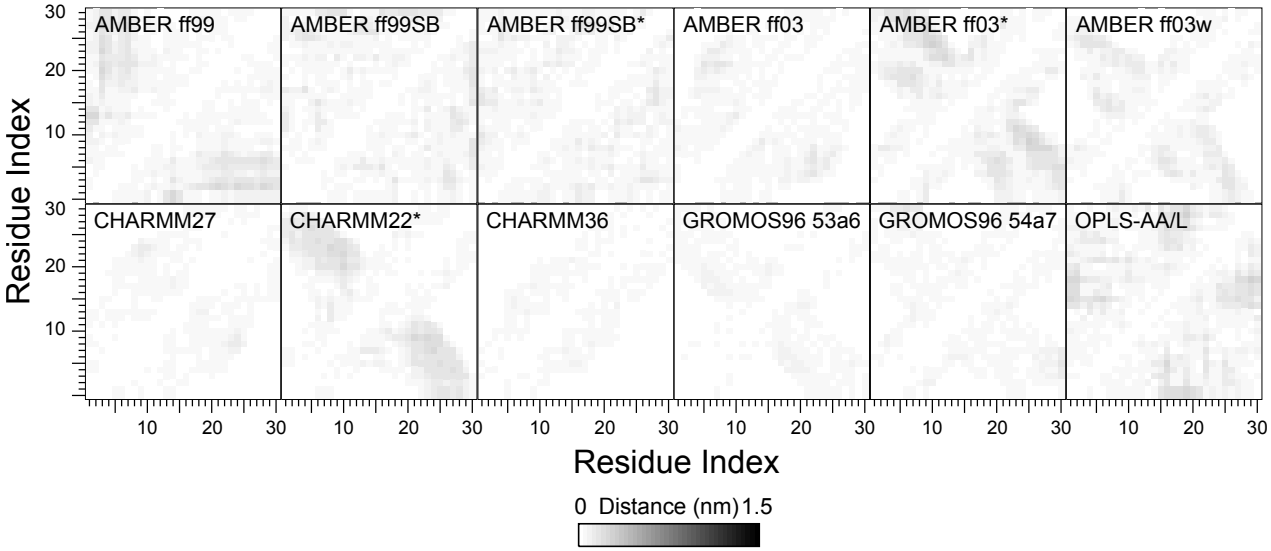

Figure S2: Sampling error in residue contact maps for Q_{30} in water at 298 K.

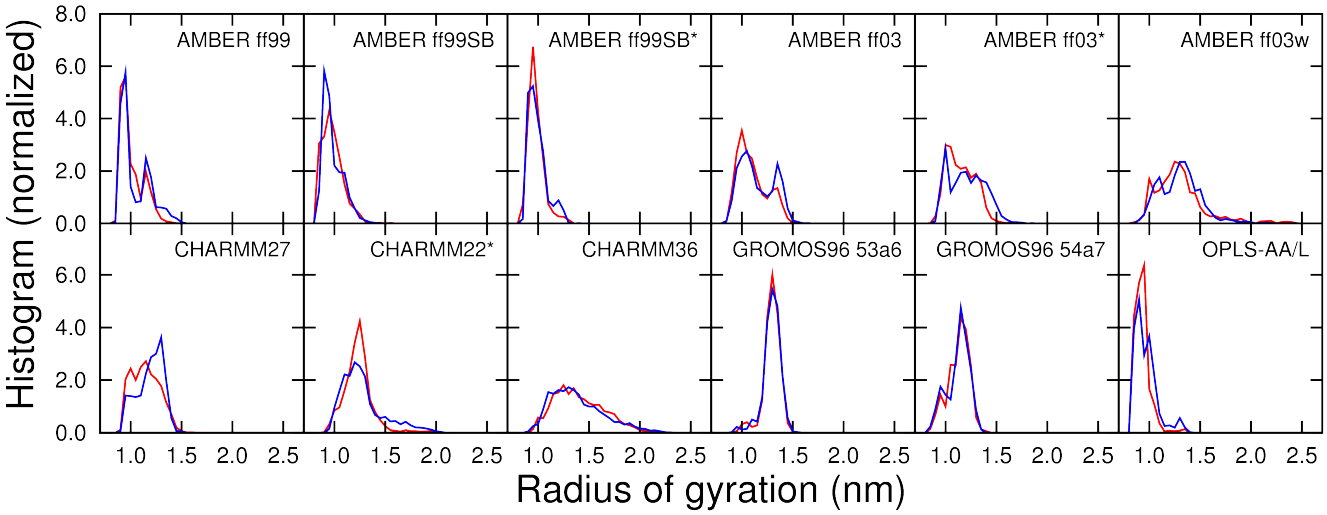

Figure S3: Block histograms of radius of gyration of Q_{30} in water at 298 K: first 50 ns (red), last 50 ns (blue).

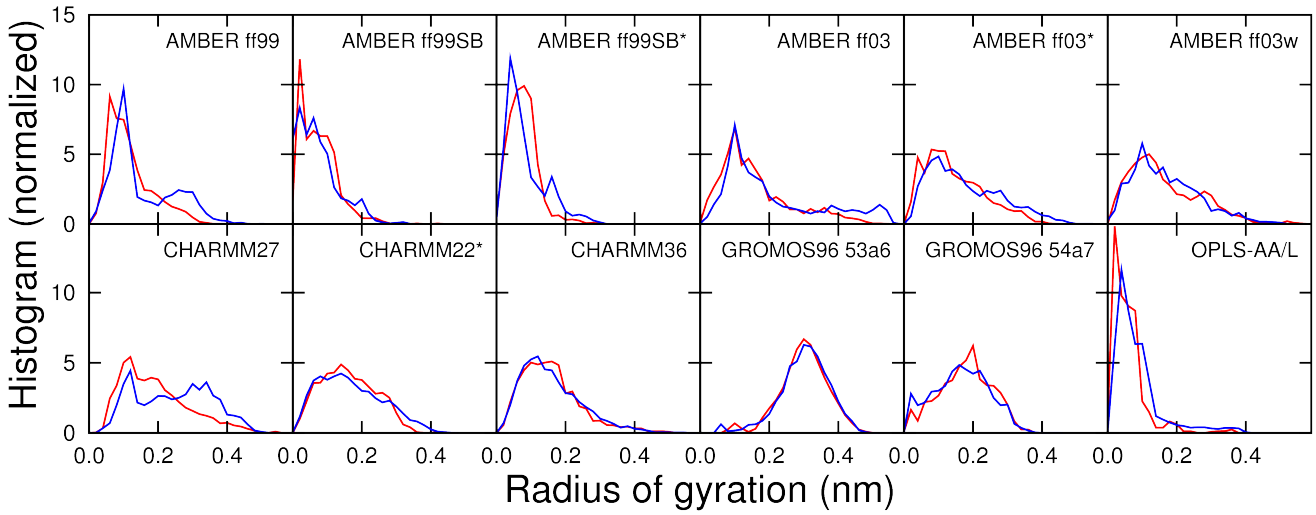

Figure S4: Block histograms of asphericity of Q_{30} in water at 298 K: first 50 ns (red), last 50 ns (blue).

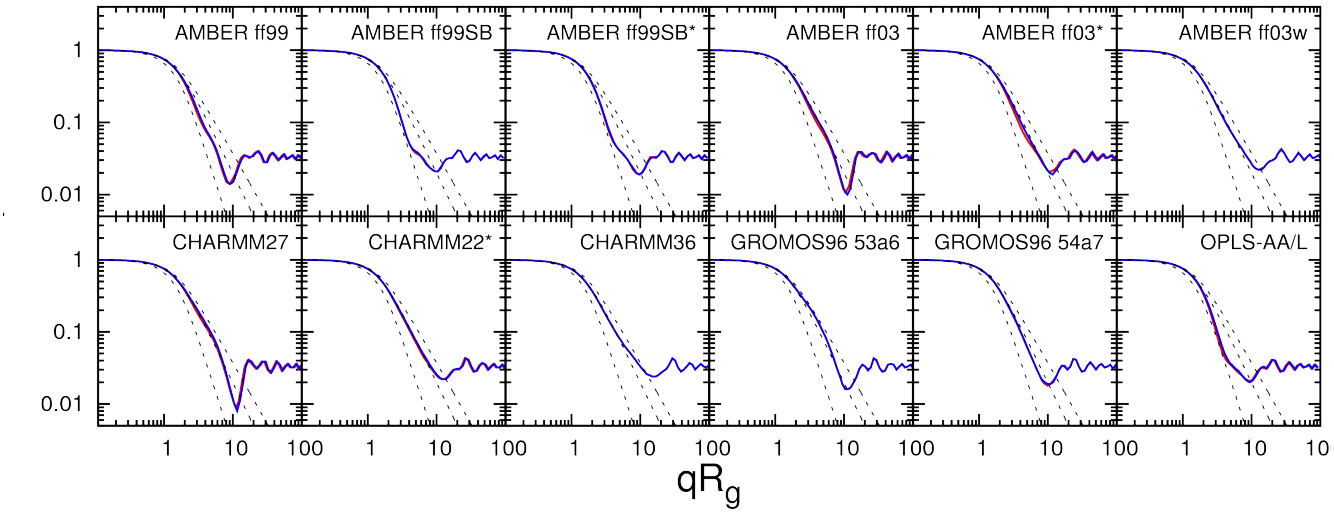

Figure S5: Single chain form factor of Q_{30} in water at 298 K: first 50 ns (red), last 50 ns (blue). Dashed lines indicate analytical predictions for (left to right) $\nu = 1/3$, $\nu = 1/2$, $\nu = 0.588$.

Force field	$\langle\tau\rangle$ (ns)
AMBER ff99	3.0
AMBER ff99SB	3.6
AMBER ff99SB*	3.3
AMBER ff03	5.5
AMBER ff03*	3.5
AMBER ff03w	0.9
CHARMM27	8.7
CHARMM22*	2.4
CHARMM36	1.5
GROMOS96 53a6	1.4
GROMOS96 54a7	5.7
OPLS-AA/L	2.2

Table S4: Conformational relaxation time of Q_{30} in water. In each set of simulations, the trajectories were unmixed (i.e., the configurational swaps were undone). For each unmixed trajectory, we calculated the structural RMSD autocorrelation function (RMSD calculation over all atoms of Q_{30} and with respect to the initial configurations for production simulations) and fit it to a function of the form $y = \exp(-x/\tau)$. The values in the table are averaged over all replicas for each force field.

SUPERHEATING OF WATER

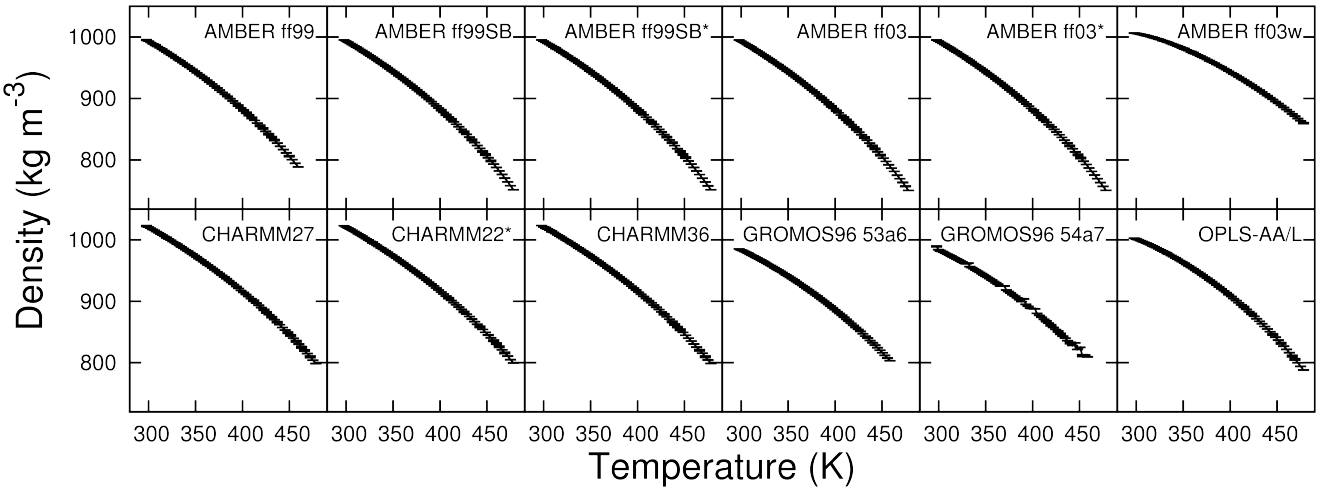

Figure S6: Average density of the system as a function of temperature.

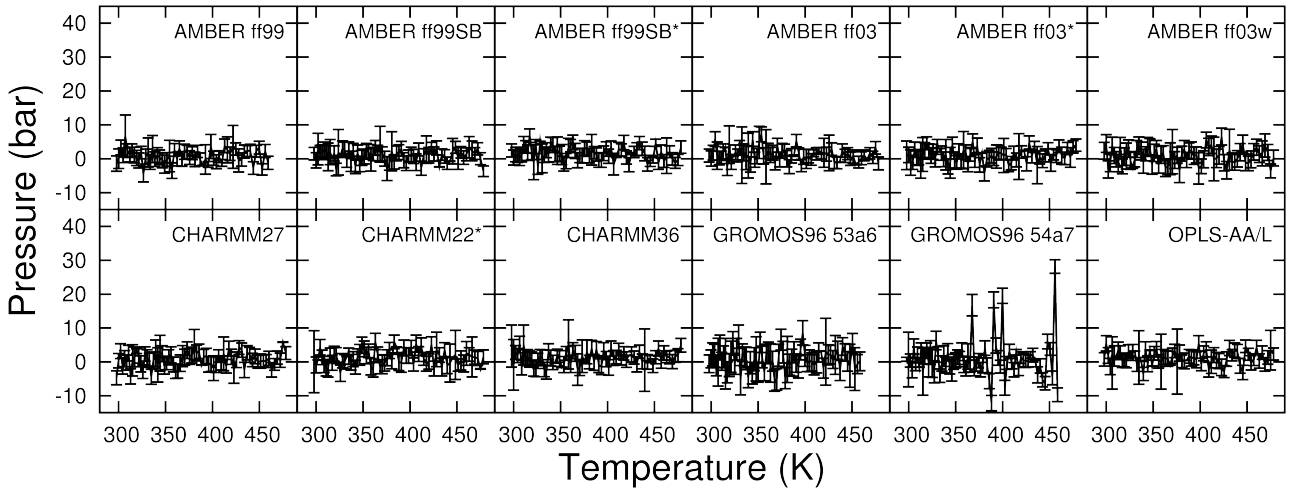

Figure S7: Average pressure of the system as a function of temperature.

SOLVATION THERMODYNAMICS

Force field	Water model	Propionamide	N-methylamide	Zwitterionic glutamine	Neutral glutamine	Ref.
AMBER ff94 (1)	TIP3P	–32.2				(2)
AMBER ff99	TIP3P	–42.2				(3)
AMBER ff03	TIP3P	–43.9				(4)
CHARMM22 (5)	TIP3P	–31.4				(2)
CHARMM22	TIP3P for CHARMM		–49.4			(6)
GROMOS96 53a6	SPC	–42.3				(3)
OPLS-AA (1996) (7)	TIP3P	–35.1				(2)
OPLS-AA/L	TIP4P	–35.5				(8)
OPLS-AA/L	TIP4P	–32.9				(3)
OPLS-AA/L	TIP4P			–249.4	–79.9	(9)

Table S5: Hydration free energies (in kJ/mol) of propionamide, the analog of the glutamine side chain; N-methylacetamide, an analog of the peptide backbone; zwitterionic glutamine; and neutral (uncharged) glutamine.

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