Supplemental Information

Solvation Thermodynamics of Oligoglycine with Respect to Chain Length and Flexibility

Justin A. Drake, Robert C. Harris, and B. Montgomery Pettitt

Supporting Material

Solvation thermodynamics of oligoglycine with respect to chain length
and flexibility: implications for aggregation and collapse

JA Drake[1], RC Harris[2], and BM Pettitt[1][*]

[1] Department of Biochemistry and Molecular Biology, Sealy Center for Structural Biology and
Molecular Biophysics, University of Texas Medical Branch, 301 University Blvd, Galveston,
Texas, 77555-0304

[2] Department of Chemistry, Temple University, 1801 N Broad St, Philadelphia PA 19122

[*]Corresponding Author: BM Pettitt
Email: bmpettitt@utmb.edu
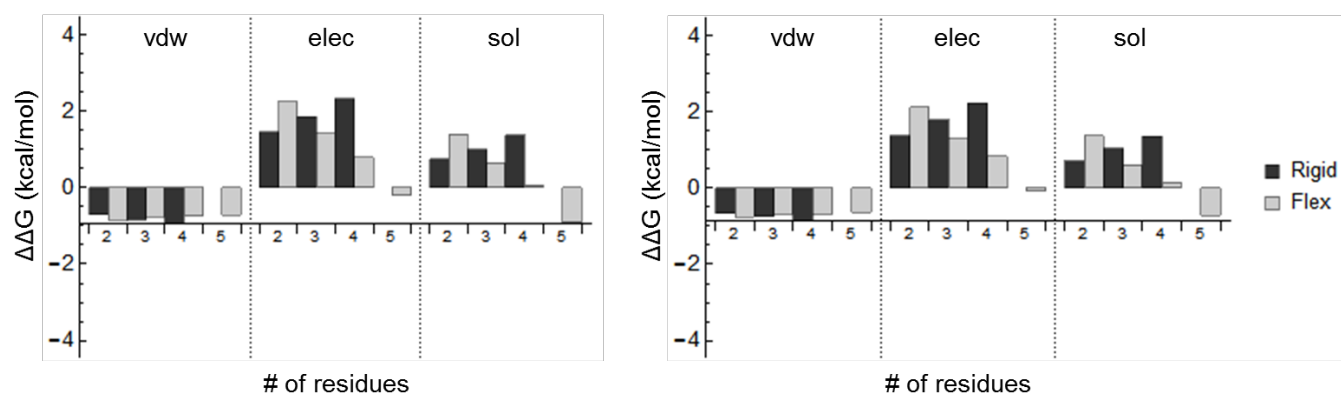
Figure S1: Differences in solvation free energy and its vdw and elec components between C36 and ff12SB at 300K (left) and 320K (right). Black and gray bars are the results for the rigid and flexible oligoglycine models, respectively
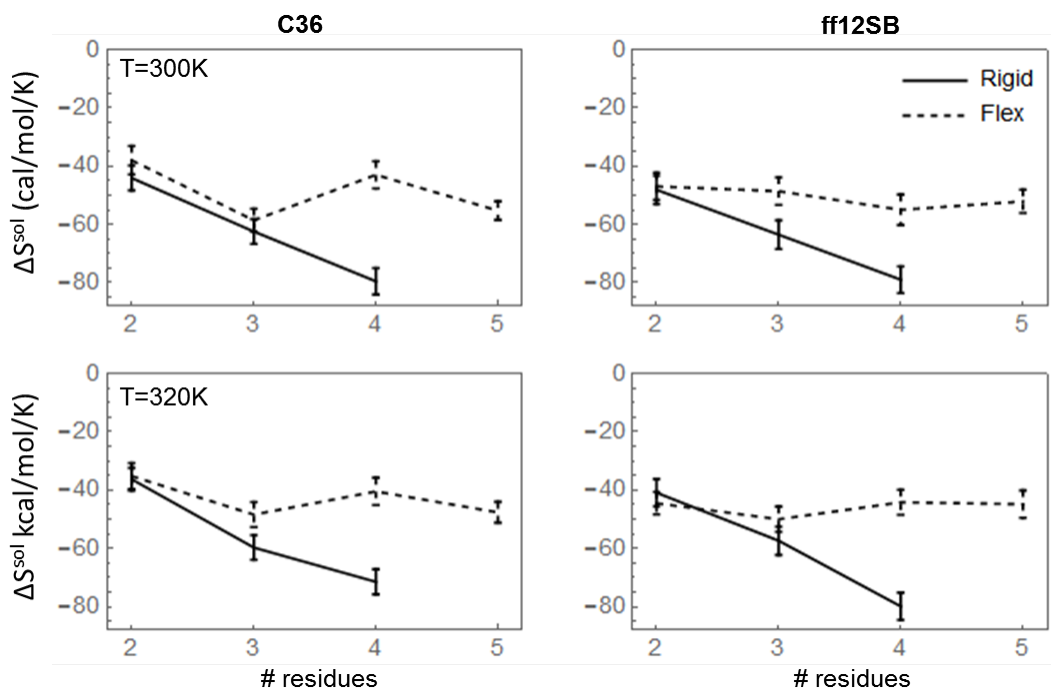
Figure S2: Solvation entropy calculated by the end point energy approach (see Methods) at 300K (top row) and 320K (bottom row) with the C36 (left) and ff12SB (right) force fields.
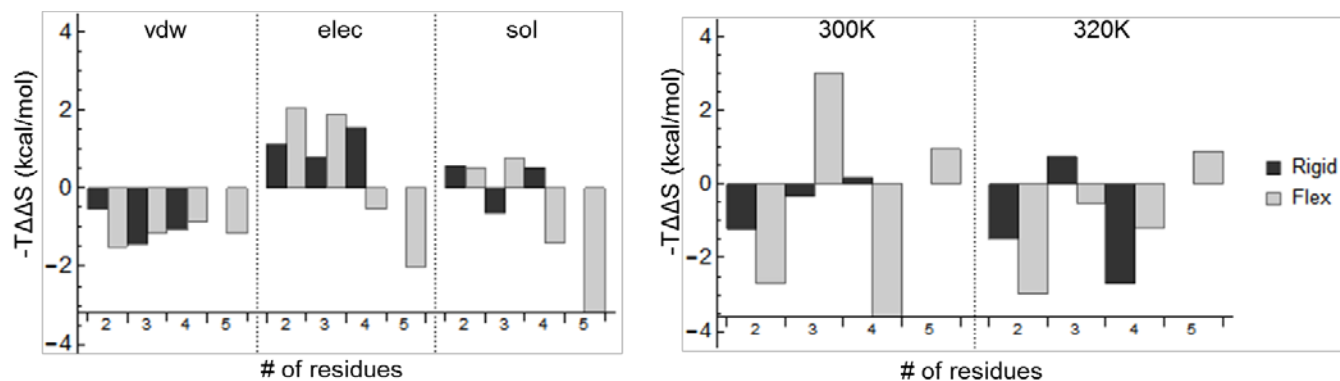
Figure S3: Differences in solvation entropy and its vdw and elec components between C36 and ff12SB calculated at 310K using the finite difference approach (left). Black and gray bars are the results for the rigid and flexible oligoglycine models, respectively. The right figure shows differences in the overall solvation entropy between force fields at 300K and 320K from the end point energy approach.
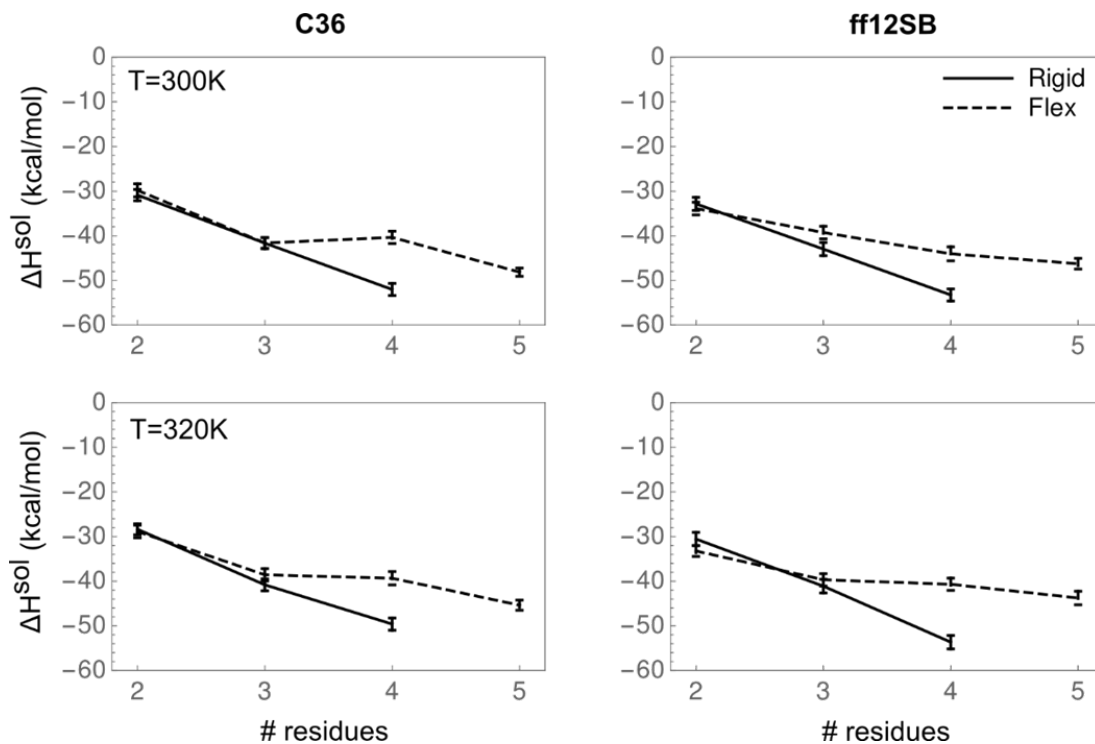
Figure S4: Solvation enthalpy calculated by the end point energy approach at 300K (top row) and 320K (bottom row) with the C36 (left) and ff12SB (right) force fields.
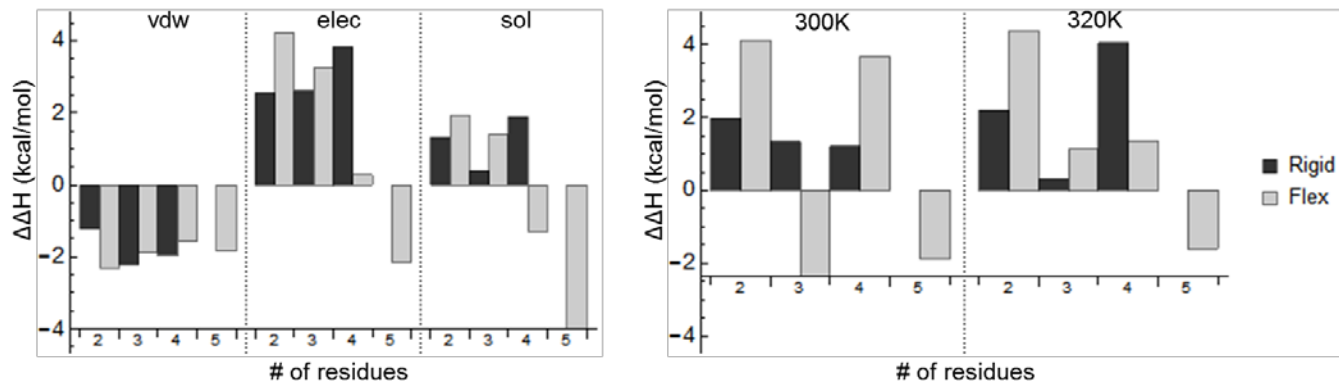
Figure S5: Differences in solvation enthalpy and its vdw and elec components between C36 and ff12SB calculated at 310K using the finite difference approach (left). Black and gray bars are the results for the rigid and flexible oligoglycine models, respectively. The right figure shows differences in the overall solvation enthalpy between force fields at 300K and 320K from the end point energy approach.

Table S1: Oligoglycine solvation free energies

CHARMM36

N	Temp.	ΔG_{flex}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	ΔG_{fix}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	$\Delta\Delta G^{vdw}$
2	300	0.149	0.031	0.009	−0.203	0.023	0.010	−0.352
	320	0.771	0.024	0.011	0.442	0.023	0.011	−0.329
3	300	−0.034	0.034	0.018	−0.842	0.031	0.013	−0.808
	320	0.641	0.032	0.012	−0.002	0.034	0.011	−0.643
4	300	−0.558	0.039	0.023	−1.483	0.032	0.014	−0.925
	320	0.169	0.039	0.019	−0.491	0.037	0.012	−0.660
5	300	−0.998	0.065	0.024				
	320	−0.234	0.051	0.018				

N	Temp.	ΔG_{flex}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	ΔG_{fix}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	$\Delta\Delta G^{elec}$
2	300	−18.580	0.052	0.012	−17.461	0.021	0.008	1.119
	320	−18.389	0.043	0.011	−17.204	0.023	0.009	1.185
3	300	−24.014	0.352	0.049	−22.079	0.024	0.010	1.935
	320	−23.718	0.263	0.046	−21.705	0.024	0.008	2.013
4	300	−26.926	0.653	0.129	−26.700	0.036	0.011	0.226
	320	−26.568	0.479	0.096	−26.247	0.023	0.010	0.321
5	300	−30.564	1.035	0.238				
	320	−29.900	1.010	0.135				

N	Temp.	ΔG_{flex}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	ΔG_{fix}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	$\Delta\Delta G^{sol}$
2	300	−18.431	0.060	0.015	−17.664	0.031	0.013	0.767
	320	−17.618	0.049	0.016	−16.762	0.033	0.014	0.856
3	300	−24.048	0.354	0.052	−22.921	0.039	0.016	1.127
	320	−23.078	0.265	0.048	−21.708	0.042	0.014	1.370
4	300	−27.485	0.654	0.131	−28.182	0.049	0.018	−0.697
	320	−26.400	0.481	0.098	−26.738	0.043	0.016	−0.338
5	300	−31.562	1.037	0.239				
	320	−30.134	1.012	0.136				

Amber ff12SB

N	Temp.	ΔG_{flex}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	ΔG_{fix}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	$\Delta\Delta G^{vdw}$
2	300	1.000	0.029	0.012	0.498	0.026	0.011	−0.502
	320	1.530	0.029	0.010	1.110	0.022	0.012	−0.417
3	300	0.727	0.035	0.011	−0.003	0.027	0.014	−0.730
	320	1.330	0.031	0.011	0.744	0.027	0.013	−0.583
4	300	0.178	0.043	0.021	−0.538	0.033	0.015	−0.716
	320	0.849	0.039	0.016	0.386	0.036	0.014	−0.463
5	300	−0.283	0.058	0.021				
	320	0.406	0.054	0.026				

N	Temp.	ΔG_{flex}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	ΔG_{fix}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	$\Delta\Delta G^{elec}$
2	300	−20.835	0.097	0.015	−18.918	0.016	0.008	1.917
	320	−20.512	0.086	0.016	−18.588	0.019	0.008	1.924
3	300	−25.433	0.279	0.040	−23.927	0.021	0.009	1.506
	320	−25.014	0.267	0.039	−23.502	0.033	0.010	1.512
4	300	−27.729	0.473	0.076	−29.029	0.027	0.011	−1.300
	320	−27.406	0.351	0.066	−28.476	0.021	0.012	−1.070
5	300	−30.362	1.016	0.116				
	320	−29.828	0.632	0.085				

N	Temp.	ΔG_{flex}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	ΔG_{fix}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	$\Delta\Delta G^{sol}$
2	300	−19.834	0.101	0.019	−18.420	0.030	0.014	1.414
	320	−18.987	0.090	0.019	−17.481	0.029	0.014	1.506
3	300	−24.706	0.282	0.041	−23.930	0.034	0.017	0.776
	320	−23.687	0.269	0.041	−22.758	0.043	0.016	0.929
4	300	−27.550	0.475	0.079	−29.567	0.043	0.019	−2.017
	320	−26.556	0.353	0.068	−28.089	0.042	0.018	−1.533
5	300	−30.645	1.017	0.118				
	320	−29.422	0.635	0.089				

Solvation free energies of Gly$_{2-5}$ either fixed in a rigid-extended conformation (subscript "fix") or allowed to sample conformation space with no physical constraints (subscript "flex") at 300K and 320K. Results for the van der Waals (vdw), electrostatic (elec), and overall (sol) solvation free energies are reported from top to bottom in units of kcal/mol for the C36 (left) and Amber ff12SB (right) force fields. $\Delta\Delta G's$ are provided as the difference between ΔG_{fix} and ΔG_{flex} for each component and the overall solvation free energy at both temperatures. N is the number of glycine residues, σ_{ACF}^{vdw} and σ_{ACF}^{elec} are the errors in ΔG^{vdw} and ΔG^{elec}, respectively, calculated from an autocorrelation time analysis (see Methods), and σ_{BSE}^{vdw} and σ_{BSE}^{elec} are the errors in ΔG^{vdw} and ΔG^{elec}, respectively, calculated from a block standard error

analysis. Error propagation was used to compute $\sigma_{ACF}^{sol} = \sqrt{(\sigma_{ACF}^{vdw})^2 + (\sigma_{ACF}^{elec})^2}$ and $\sigma_{BSE}^{sol} =$

$$\sqrt{(\sigma_{BSE}^{vdw})^2 + (\sigma_{BSE}^{elec})^2}$$

Table S2: Oligoglycine solvation entropies calculated by the finite difference approach

CHARMM36

	Flexible			Rigid/Ext			
N	ΔS_{flex}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	ΔS_{fix}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	$\Delta\Delta S^{vdw}$
2	−31.10	1.96	0.71	−32.25	1.63	0.74	−1.15
3	−33.75	2.33	1.08	−42.00	2.30	0.85	−8.25
4	−36.35	2.76	1.49	−49.60	2.45	0.92	−13.25
5	−38.20	4.13	1.50				
N	ΔS_{flex}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	ΔS_{fix}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	$\Delta\Delta S^{elec}$
2	−9.55	3.37	0.81	−12.85	1.56	0.60	−3.30
3	−14.80	21.97	3.36	−18.70	1.70	0.64	−3.90
4	−17.90	40.49	8.04	−22.65	2.14	0.74	−4.75
5	−33.20	72.31	13.68				
N	ΔS_{flex}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	ΔS_{fix}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	$\Delta\Delta S^{sol}$
2	−40.65	3.87	1.08	−45.10	2.26	0.96	−4.45
3	−48.50	22.11	3.53	−60.65	2.87	1.07	−12.15
4	−54.25	40.59	8.18	−72.20	3.26	1.18	−17.95
5	−71.40	72.45	13.76				

Amber ff12SB

	Flexible			Rigid/Ext			
N	ΔS_{flex}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	ΔS_{fix}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	$\Delta\Delta S^{vdw}$
2	−26.25	2.05	0.78	−30.50	1.70	0.81	−4.25
3	−30.00	2.34	0.78	−37.37	1.91	0.96	−7.37
4	−33.55	2.90	1.32	−46.20	2.44	1.03	−12.65
5	−34.45	3.96	1.67				
N	ΔS_{flex}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	ΔS_{fix}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	$\Delta\Delta S^{elec}$
2	−16.15	6.48	1.10	−16.50	1.24	0.57	−0.35
3	−20.95	19.31	2.79	−21.25	1.96	0.67	−0.30
4	−16.15	29.45	5.03	−27.65	1.71	0.81	−11.50
5	−26.70	59.83	7.19				
N	ΔS_{flex}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	ΔS_{fix}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	$\Delta\Delta S^{sol}$
2	−42.35	6.76	1.35	−46.95	2.09	0.99	−4.60
3	−50.95	19.49	2.90	−58.60	2.74	1.17	−7.65
4	−49.70	29.59	5.20	−73.90	3.01	1.31	−24.20
5	−61.15	59.95	7.38				

Solvation entropies of rigid and flexible Gly$_{2-5}$ calculated by the finite difference approach (FD). Results for the vdw, elec, and overall solvation entropies are given from top to bottom for C36 (left) and ff12SB (right). Units are in cal/mol/K. Errors in ΔS^{vdw}, ΔS^{elec}, and ΔS^{sol} were calculated by propagating, separately, the ACF and BSE errors in ΔG^{vdw}, ΔG^{elec}, and ΔG^{sol}. $\Delta\Delta S's$ are provided as the difference between ΔS_{fix} and ΔS_{flex}.

Table S3: Oligoglycine solvation entropies calculated by the end point energy approach

CHARMM36

		Flexible			Rigid/Ext			
N	Temp.	ΔS_{flex}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	ΔS_{fix}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	$\Delta\Delta S^{sol}$
2	300	−37.970	8.349	4.880	−44.063	7.461	4.244	−6.093
	320	−35.159	7.748	4.435	−36.266	8.073	3.875	−1.106
3	300	−58.583	8.301	3.944	−62.440	8.224	4.227	−3.857
	320	−48.397	8.105	4.328	−59.694	8.101	4.200	−11.297
4	300	−42.957	7.243	4.670	−79.540	7.778	4.554	−36.583
	320	−40.438	7.606	4.697	−71.469	8.042	4.275	−31.031
5	300	−55.280	8.056	3.214				
	320	−47.609	7.293	3.575				

Amber ff12SB

		Flexible			Rigid/Ext			
N	Temp.	ΔS_{flex}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	ΔS_{fix}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	$\Delta\Delta S^{sol}$
2	300	−46.937	8.397	4.727	−48.120	7.067	4.874	−1.183
	320	−44.500	7.608	3.854	−40.869	7.579	4.710	3.631
3	300	−48.573	8.489	4.742	−63.540	8.481	4.914	−14.967
	320	−49.981	7.870	4.330	−57.369	8.651	4.828	−7.388
4	300	−54.993	7.623	5.230	−78.983	7.851	4.570	−23.990
	320	−44.156	8.602	4.318	−79.888	7.192	4.703	−35.731
5	300	−52.093	7.727	4.029				
	320	−44.809	7.535	4.718				

Solvation entropies of rigid and flexible Gly$_{2-5}$ calculated by the end point energy (EP) approach at 300K and 320K with the C36 (left) and ff12SB (right) force fields. Errors in ΔG^{sol} were propagated with those in ΔH^{sol} estimated by the EP approach at both temperatures to yield error estimates of ΔS^{sol}. $\Delta\Delta S's$ are provided as the difference between ΔS_{fix} and ΔS_{flex}.

Table S4: Oligoglycine solvation enthalpies calculated by the finite difference approach

CHARMM36

N	ΔH_{flex}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	ΔH_{fix}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	$\Delta\Delta H^{vdw}$
2	−9.18	0.61	0.22	−9.88	0.50	0.23	−0.70
3	−10.16	0.72	0.34	−13.44	0.71	0.26	−3.28
4	−11.46	0.86	0.46	−16.36	0.76	0.29	−4.90
5	−12.46	1.28	0.47				

N	ΔH_{flex}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	ΔH_{fix}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	$\Delta\Delta H^{elec}$
2	−21.44	1.05	0.25	−21.32	0.48	0.19	0.13
3	−28.45	6.82	1.04	−27.69	0.53	0.20	0.76
4	−32.30	12.56	2.49	−33.49	0.66	0.23	−1.20
5	−40.52	22.43	4.24				

N	ΔH_{flex}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	ΔH_{fix}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	$\Delta\Delta H^{sol}$
2	−30.63	1.20	0.34	−31.19	0.70	0.30	−0.57
3	−38.60	6.86	1.10	−41.12	0.89	0.33	−2.52
4	−43.76	12.59	2.54	−49.84	1.01	0.37	−6.08
5	−52.98	22.47	4.27				

Amber ff12SB

N	ΔH_{flex}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	ΔH_{fix}^{vdw}	σ_{ACF}^{vdw}	σ_{BSE}^{vdw}	$\Delta\Delta H^{vdw}$
2	−6.87	0.64	0.24	−8.65	0.53	0.25	−1.78
3	−8.27	0.73	0.24	−11.21	0.59	0.30	−2.94
4	−9.89	0.90	0.41	−14.40	0.76	0.32	−4.51
5	−10.62	1.23	0.52				

N	ΔH_{flex}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	ΔH_{fix}^{elec}	σ_{ACF}^{elec}	σ_{BSE}^{elec}	$\Delta\Delta H^{elec}$
2	−25.68	2.01	0.34	−23.87	0.39	0.18	1.81
3	−31.72	5.99	0.87	−30.30	0.61	0.21	1.42
4	−32.57	9.14	1.56	−37.32	0.53	0.25	−4.75
5	−38.37	18.56	2.23				

N	ΔH_{flex}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	ΔH_{fix}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	$\Delta\Delta H^{sol}$
2	−32.54	2.10	0.42	−32.51	0.65	0.31	0.03
3	−39.99	6.04	0.90	−41.51	0.85	0.36	−1.52
4	−42.46	9.18	1.61	−51.74	0.93	0.41	−9.28
5	−48.99	18.60	2.29				

Solvation enthalpies of rigid and flexible Gly$_{2-5}$ calculated by the FD approach at 310K. Results for the vdw, elec, and overall solvation enthalpy are given from top to bottom for C36 (left) and ff12SB (right). Units are in kcal/mol. Errors in ΔH^{vdw}, ΔH^{elec}, and ΔH^{sol} were calculated by propagating, separately, the ACF and BSE errors in ΔG^{vdw}, ΔG^{elec}, and ΔG^{sol}. $\Delta\Delta H's$ are provided as the difference between ΔH_{fix} and ΔH_{flex}.

Table S5: Oligoglycine solvation enthalpies calculated by the end point energy approach

| | | CHARMM36 | | | | | | | | | Amber ff12SB | | | | | | |
| | | Flexible | | | Rigid/Ext | | | | | | Flexible | | | Rigid/Ext | | | |
N	Temp.	ΔH_{flex}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	ΔH_{fix}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	$\Delta\Delta H^{sol}$	N	Temp.	ΔH_{flex}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	ΔH_{fix}^{sol}	σ_{ACF}^{sol}	σ_{BSE}^{sol}	$\Delta\Delta H^{sol}$
2	300	−29.822	2.504	1.464	−30.883	2.238	1.273	−1.061	2	300	−33.915	2.517	1.418	−32.856	2.120	1.462	1.059
	320	−28.869	2.479	1.419	−28.367	2.583	1.240	0.502		320	−33.227	2.433	1.233	−30.559	2.425	1.507	2.668
3	300	−41.623	2.465	1.182	−41.653	2.467	1.268	−0.030	3	300	−39.278	2.531	1.422	−42.992	2.544	1.474	−3.714
	320	−38.565	2.580	1.384	−40.810	2.592	1.344	−2.245		320	−39.681	2.504	1.385	−41.116	2.768	1.545	−1.435
4	300	−40.372	2.072	1.395	−52.044	2.333	1.366	−11.672	4	300	−44.048	2.237	1.567	−53.262	2.355	1.371	−9.214
	320	−39.340	2.386	1.500	−49.608	2.573	1.368	−10.268		320	−40.686	2.730	1.380	−53.653	2.301	1.505	−12.967
5	300	−48.146	2.183	0.934					5	300	−46.273	2.083	1.203				
	320	−45.369	2.103	1.136						320	−43.761	2.326	1.507				

Solvation enthalpies of rigid and flexible Gly$_{2\text{-}5}$ calculated by the end point energy approach at 300K and 320K with C36 (left) and ff12SB (right). Errors in ΔH^{sol} (σ_{BSE}^{sol}, σ_{BSE}^{sol}) were directly calculated and the details can be found in the Methods section and Appendix A. Units are in kcal/mol and $\Delta\Delta H's$ are provided as the difference between ΔH_{fix} and ΔH_{flex}.

Table S6: Solvation thermodynamics calculated by the finite difference approach at 310K

	CHARMM36								
	Flexible			**Rigid/Ext**					
N	ΔG_{flex}^{vdw}	ΔH_{flex}^{vdw}	$-T\Delta S_{flex}^{vdw}$	ΔG_{fix}^{vdw}	ΔH_{fix}^{vdw}	$-T\Delta S_{fix}^{vdw}$	$\Delta\Delta G^{vdw}$	$\Delta\Delta H^{vdw}$	$-T\Delta\Delta S^{vdw}$
2	0.46	−9.18	9.64	0.12	−9.88	10.00	−0.34	−0.70	0.35
3	0.30	−10.16	10.46	−0.42	−13.44	13.02	−0.73	−3.28	2.56
4	−0.19	−11.46	11.27	−0.99	−16.36	15.38	−0.79	−4.90	4.11
5	−0.62	−12.46	11.84						
N	ΔG_{flex}^{elec}	ΔH_{flex}^{elec}	$-T\Delta S_{flex}^{elec}$	ΔG_{fix}^{elec}	ΔH_{fix}^{elec}	$-T\Delta S_{fix}^{elec}$	$\Delta\Delta G^{elec}$	$\Delta\Delta H^{elec}$	$-T\Delta\Delta S^{elec}$
2	−18.48	−21.44	2.96	−17.33	−21.32	3.98	1.15	0.13	1.02
3	−23.87	−28.45	4.59	−21.89	−27.69	5.80	1.97	0.76	1.21
4	−26.75	−32.30	5.55	−26.47	−33.49	7.02	0.27	−1.20	1.47
5	−30.23	−40.52	10.29						
N	ΔG_{flex}^{sol}	ΔH_{flex}^{sol}	$-T\Delta S_{flex}^{sol}$	ΔG_{fix}^{sol}	ΔH_{fix}^{sol}	$-T\Delta S_{fix}^{sol}$	$\Delta\Delta G^{sol}$	$\Delta\Delta H^{sol}$	$-T\Delta\Delta S^{sol}$
2	−18.02	−30.63	12.60	−17.21	−31.19	13.98	0.81	−0.57	1.38
3	−23.56	−38.60	15.03	−22.31	−41.12	18.80	1.25	−2.52	3.77
4	−26.94	−43.76	16.82	−27.46	−49.84	22.38	−0.52	−6.08	5.56
5	−30.85	−52.98	22.13						

	Amber ff12SB								
	Flexible			**Rigid/Ext**					
N	ΔG_{flex}^{vdw}	ΔH_{flex}^{vdw}	$-T\Delta S_{flex}^{vdw}$	ΔG_{fix}^{vdw}	ΔH_{fix}^{vdw}	$-T\Delta S_{fix}^{vdw}$	$\Delta\Delta G^{vdw}$	$\Delta\Delta H^{vdw}$	$-T\Delta\Delta S^{vdw}$
2	1.26	−6.87	8.14	0.80	−8.65	9.46	−0.46	−1.78	1.32
3	1.03	−8.27	9.30	0.37	−11.21	11.58	−0.66	−2.94	2.28
4	0.51	−9.89	10.40	−0.08	−14.40	14.32	−0.59	−4.51	3.92
5	0.06	−10.62	10.68						
N	ΔG_{flex}^{elec}	ΔH_{flex}^{elec}	$-T\Delta S_{flex}^{elec}$	ΔG_{fix}^{elec}	ΔH_{fix}^{elec}	$-T\Delta S_{fix}^{elec}$	$\Delta\Delta G^{elec}$	$\Delta\Delta H^{elec}$	$-T\Delta\Delta S^{elec}$
2	−20.67	−25.68	5.01	−18.75	−23.87	5.11	1.92	1.81	0.11
3	−25.22	−31.72	6.49	−23.71	−30.30	6.59	1.51	1.42	0.09
4	−27.57	−32.57	5.01	−28.75	−37.32	8.57	−1.18	−4.75	3.57
5	−30.10	−38.37	8.28						
N	ΔG_{flex}^{sol}	ΔH_{flex}^{sol}	$-T\Delta S_{flex}^{sol}$	ΔG_{fix}^{sol}	ΔH_{fix}^{sol}	$-T\Delta S_{fix}^{sol}$	$\Delta\Delta G^{sol}$	$\Delta\Delta H^{sol}$	$-T\Delta\Delta S^{sol}$
2	−19.41	−32.54	13.13	−17.95	−32.51	14.55	1.46	0.03	1.43
3	−24.20	−39.99	15.79	−23.34	−41.51	18.17	0.85	−1.52	2.37
4	−27.05	−42.46	15.41	−28.83	−51.74	22.91	−1.77	−9.28	7.50
5	−30.03	−48.99	18.96						

Solvation thermodynamics of rigid and flexible Gly$_{2-5}$ calculated by the FD approach at 310K. Results for each component and the overall solvation free energy are shown from top to bottom within each panel for C36 (top panel) and ff12SB (bottom panel). ΔG^{sol} at 310K was approximated as the average of ΔG^{sol}

at 300K and 320K. Differences in each thermodynamic quantity between the rigid and flexible

oligoglycine models are shown on the right side of each panel. All units are in kcal/mol.

Table S7: Solvation thermodynamics calculated by the end point energy approach at 300K and 320K

CHARMM36 (300K)

N	ΔG_{flex}^{sol}	ΔH_{flex}^{sol}	$-T\Delta S_{flex}^{sol}$	ΔG_{fix}^{sol}	ΔH_{fix}^{sol}	$-T\Delta S_{fix}^{sol}$	$\Delta\Delta G^{sol}$	$\Delta\Delta H^{sol}$	$-T\Delta\Delta S^{sol}$
2	−18.43	−29.82	11.39	−17.66	−30.88	13.22	0.77	−1.06	1.83
3	−24.05	−41.62	17.58	−22.92	−41.65	18.73	1.13	−0.03	1.16
4	−27.49	−40.37	12.89	−28.18	−52.04	23.86	−0.70	−11.67	10.98
5	−31.56	−48.15	16.58						

Amber ff12SB (300K)

N	ΔG_{flex}^{sol}	ΔH_{flex}^{sol}	$-T\Delta S_{flex}^{sol}$	ΔG_{fix}^{sol}	ΔH_{fix}^{sol}	$-T\Delta S_{fix}^{sol}$	$\Delta\Delta G^{sol}$	$\Delta\Delta H^{sol}$	$-T\Delta\Delta S^{sol}$
2	−19.83	−33.92	14.08	−18.42	−32.86	14.44	1.41	1.06	0.36
3	−24.71	−39.28	14.57	−23.93	−42.99	19.06	0.78	−3.71	4.49
4	−27.55	−44.05	16.50	−29.57	−53.26	23.70	−2.02	−9.21	7.20
5	−30.65	−46.27	15.63						

CHARMM36 (320K)

N	ΔG_{flex}^{sol}	ΔH_{flex}^{sol}	$-T\Delta S_{flex}^{sol}$	ΔG_{fix}^{sol}	ΔH_{fix}^{sol}	$-T\Delta S_{fix}^{sol}$	$\Delta\Delta G^{sol}$	$\Delta\Delta H^{sol}$	$-T\Delta\Delta S^{sol}$
2	−17.62	−28.87	11.25	−16.76	−28.37	11.61	0.86	0.50	0.35
3	−23.08	−38.57	15.49	−21.71	−40.81	19.10	1.37	−2.25	3.62
4	−26.40	−39.34	12.94	−26.74	−49.61	22.87	−0.34	−10.27	9.93
5	−30.13	−45.37	15.24						

Amber ff12SB (320K)

N	ΔG_{flex}^{sol}	ΔH_{flex}^{sol}	$-T\Delta S_{flex}^{sol}$	ΔG_{fix}^{sol}	ΔH_{fix}^{sol}	$-T\Delta S_{fix}^{sol}$	$\Delta\Delta G^{sol}$	$\Delta\Delta H^{sol}$	$-T\Delta\Delta S^{sol}$
2	−18.99	−33.23	14.24	−17.48	−30.56	13.08	1.51	2.67	−1.16
3	−23.69	−39.68	15.99	−22.76	−41.12	18.36	0.93	−1.44	2.36
4	−26.56	−40.69	14.13	−28.09	−53.65	25.56	−1.53	−12.97	11.43
5	−29.42	−43.76	14.34						

Solvation thermodynamics of rigid and flexible Gly_{2-5} calculated by the EP approach at 300K (top row)

and 320K (bottom row) with the C36 (left) and ff12SB (right) force fields. Differences in each

thermodynamic quantity between the rigid and flexible oligoglycine models are shown on the right side

of each panel. All units are in kcal/mol.