Table S1: RNA Duplex Dodecamer Unfolding Enthalpies $\Delta H^{\circ}_{\text{obs}}$ (kcal mol^{-1}) from Thermal Denaturation Monitored by uv-Absorbance Spectroscopy as a Function of Glycine Betaine Molality[a]

Sequence	%GC	0 molal	0.5 molal	1 molal	1.5 molal	2 molal
5'-r(GAAAUUAUAAAG)-3'	17	84.4 ± 4.0	85.0 ± 5.1	86.9 ± 3.9	86.2 ± 4.3	86.6 ± 4.0
5'-r(GAAAGUAUAAAG)-3'	25	84.1 ± 2.9	84.2 ± 2.7	85.7 ± 4.3	88.1 ± 3.2	83.5 ± 4.0
5'-r(GAUAGUAGAUAG)-3'	33	91.6 ± 5.0	95.1 ± 4.9	97.9 ± 3.8	99.1 ± 3.7	100.3 ± 4.5
5'-r(GAAAGUAGAAAC)-3'	33	89.9 ± 3.4	87.8 ± 3.8	93.4 ± 3.9	100.0 ± 2.6	102.1 ± 3.7
5'-r(GCAAAGUAAACG)-3'	42	86.6 ± 5.0	86.6 ± 4.0	89.7 ± 3.3	94.1 ± 4.5	94.3 ± 4.2
5'-r(GCAAAGCAAACG)-3'	50	93.7 ± 4.9	97.5 ± 4.6	103.6 ± 4.0	101.3 ± 3.3	105.2 ± 3.7
5'-r(GCAUAGCAUACG)-3'	50	97.3 ± 4.1	97.1 ± 3.4	103.1 ± 3.9	104.6 ± 3.4	109.9 ± 4.1
5'-r(GCGAAGCCAACG)-3'	67	85.7 ± 4.1	87.0 ± 3.7	91.7 ± 3.9	100.4 ± 4.3	105.5 ± 3.3
5'-r(GCGCCGCCGGCG)-3'	100	105.4 ± 3.6	114.6 ± 2.3	120.7 ± 4.2	119.1 ± 3.2	121.2 ± 3.9

[a]Enthalpies represent averages of duplicate or triplicate measurements. Enthalpy standard errors determined by propagating errors from separate unfolding trials.

Table S2: RNA Duplex Dodecamer Concentration-Normalized Transition Region Hyperchromicity (μM^{-1}) as a Function of Glycine Betaine Molality[a]

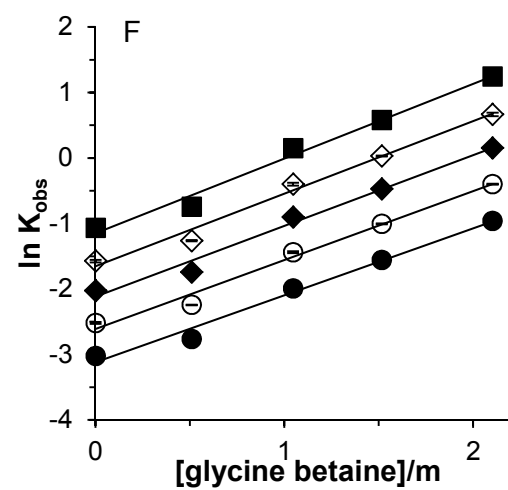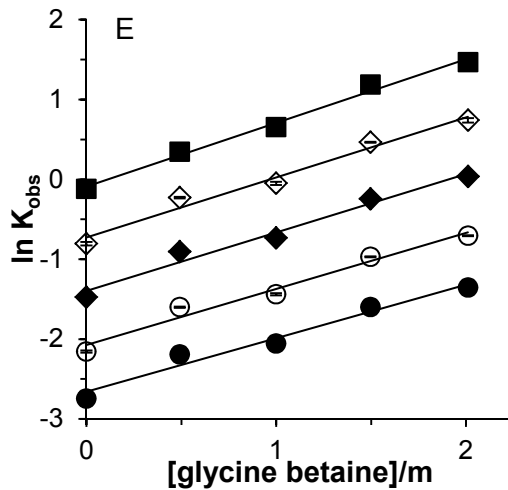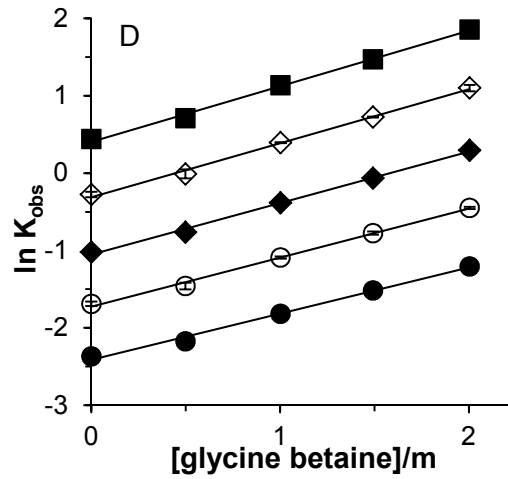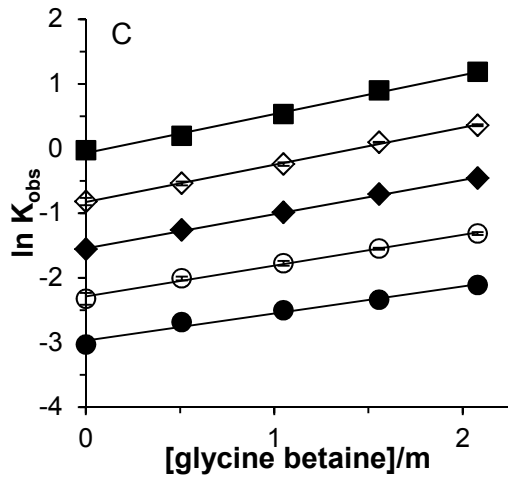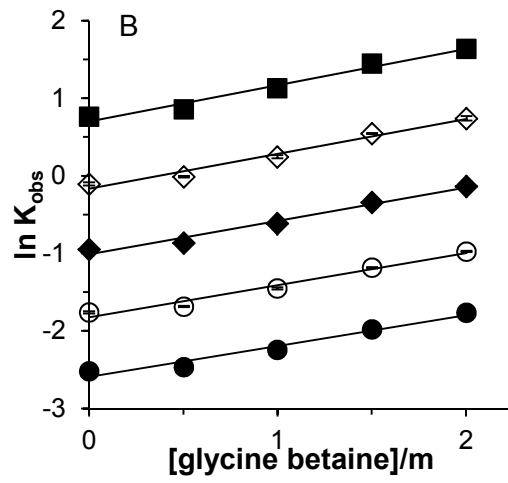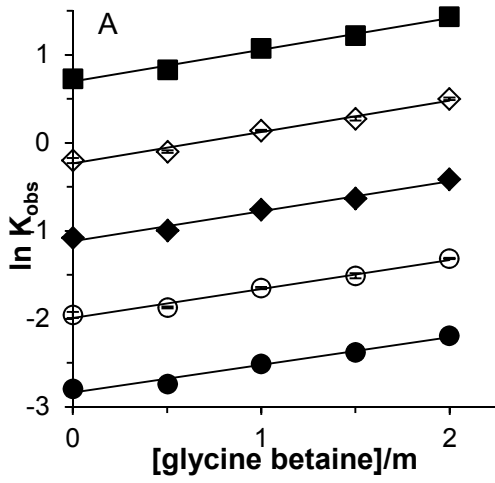| Sequence	%GC	0 molal	0.5 molal	1 molal	1.5 molal	2 molal
5'-r(GAAAUUAUAAAG)-3'	17	0.050 ± 0.001	0.050 ± 0.001	0.052 ± 0.001	0.051 ± 0.004	0.052 ± 0.001
5'-r(GAAAGUAUAAAG)-3'	25	0.050 ± 0.001	0.049 ± 0.001	0.050 ± 0.001	0.050 ± 0.003	0.052 ± 0.001
5'-r(GAUAGUAGAUAG)-3'	33	0.050 ± 0.001	0.049 ± 0.001	0.050 ± 0.001	0.050 ± 0.001	0.050 ± 0.002
5'-r(GAAAGUAGAAAC)-3'	33	0.047 ± 0.001	0.051 ± 0.001	0.052 ± 0.003	0.051 ± 0.003	0.053 ± 0.002
5'-r(GCAAAGUAAACG)-3'	42	0.046 ± 0.001	0.046 ± 0.002	0.044 ± 0.001	0.051 ± 0.001	0.046 ± 0.003
5'-r(GCAAAGCAAACG)-3'	50	0.046 ± 0.001	0.051 ± 0.001	0.050 ± 0.003	0.051 ± 0.002	0.050 ± 0.001
5'-r(GCAUAGCAUACG)-3'	50	0.044 ± 0.001	0.049 ± 0.001	0.047 ± 0.001	0.049 ± 0.001	0.055 ± 0.001
5'-r(GCGAAGCCAACG)-3'	67	0.035 ± 0.001	0.040 ± 0.001	0.040 ± 0.001	0.041 ± 0.004	0.042 ± 0.003
5'-r(GCGCCGCCGGCG)-3'	100	0.023 ± 0.002	0.028 ± 0.001	0.026 ± 0.002	0.027 ± 0.001	0.031 ± 0.001

[a]Hyperchromicities represent averages of duplicate or triplicate measurements. Standard errors determined by propagating errors from separate unfolding trials.

Table S3: Change in Solvent Accessible Surface Area (ΔASA) Values for RNA Duplex Dodecamers Assuming Stacked Nucleobases in Single Strands

sequence	%GC	total ΔASA/Å²	anionic oxygen ΔASA/Å²	sugar ΔASA/Å²	base aromatic ΔASA/Å²	base amine ΔASA/Å²	amide-like oxygen ΔASA/Å²	aliphatic base ΔASA/Å²
5'-r(GAAAUUAUAAAG)-3'	17	1112	0	5	523	330	302	0
5'-r(GAAAGUAUAAAG)-3'	25	1130	0	8	506	350	307	0
5'-r(GAUAGUAGAUAG)-3'	33	1159	0	11	481	425	277	0
5'-r(GAAAGUAGAAAC)-3'	33	1113	0	8	472	346	331	0
5'-r(GCAAAGUAAACG)-3'	42	1174	0	14	493	367	310	0
5'-r(GCAAAGCAAACG)-3'	50	1192	0	17	481	380	306	0
5'-r(GCAUAGCAUACG)-3'	50	1216	0	17	479	448	255	0
5'-r(GCGAAGCCAACG)-3'	67	1224	0	23	440	437	309	0
5'-r(GCGCCGCCGGCG)-3'	100	1301	0	35	385	527	300	0

Table S4: Change in Solvent Accessible Surface Area (ΔASA) Values for RNA Duplex Dodecamers Assuming Half-Stacked Nucleobases in Single Strands

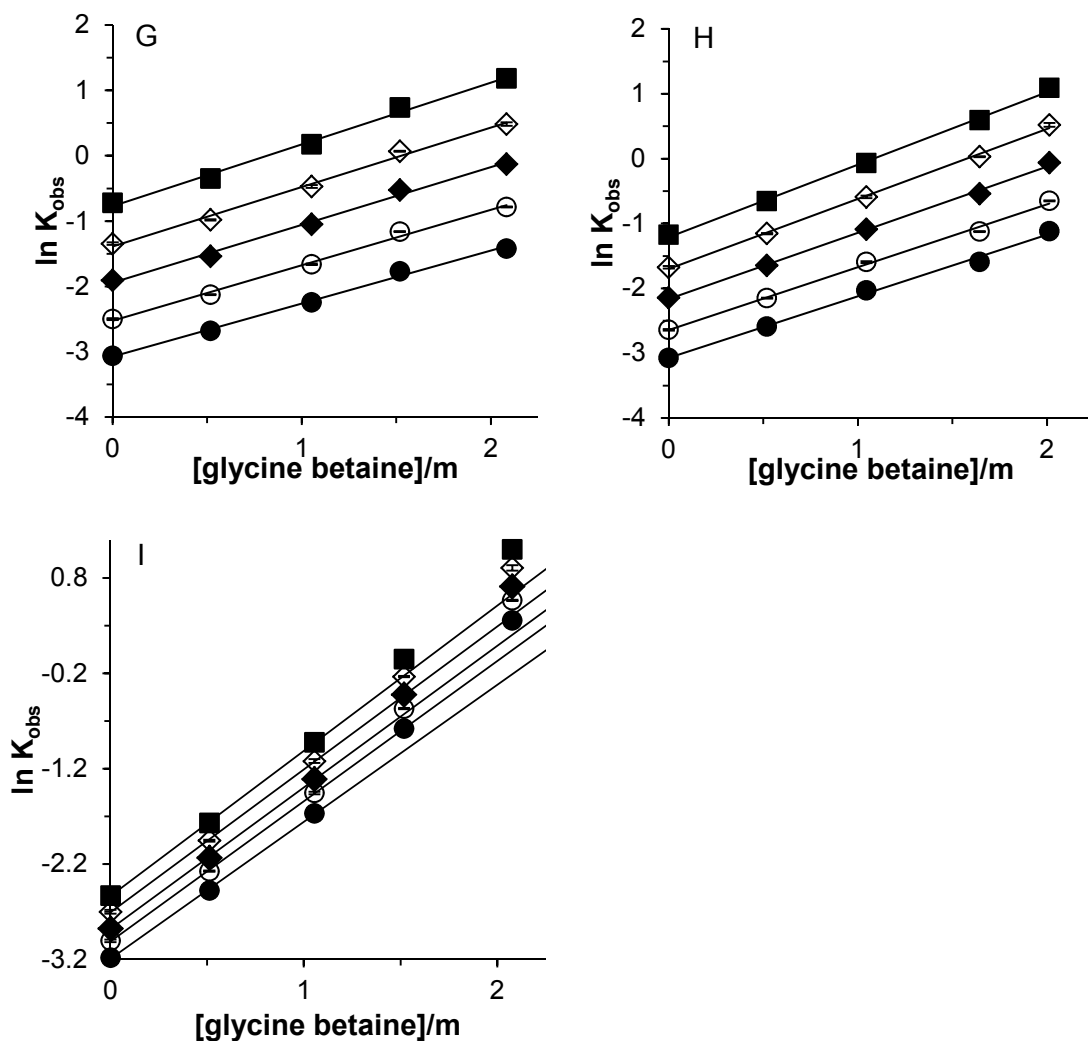| sequence	%GC	total ΔASA/Å²	anionic oxygen ΔASA/Å²	sugar ΔASA/Å²	base aromatic ΔASA/Å²	base amine ΔASA/Å²	amide-like oxygen ΔASA/Å²	aliphatic base ΔASA/Å²
5'-r(GAAAUUAUAAAG)-3'	17	2322	-174	166	1266	586	480	0
5'-r(GAAAGUAUAAAG)-3'	25	2350	-174	171	1239	623	491	0
5'-r(GAUAGUAGAUAG)-3'	33	2383	-174	177	1210	687	485	0
5'-r(GAAAGUAGAAAC)-3'	33	2363	-176	172	1206	661	502	0
5'-r(GCAAAGUAAACG)-3'	42	2406	-174	181	1199	684	517	0
5'-r(GCAAAGCAAACG)-3'	50	2432	-176	185	1177	717	530	0
5'-r(GCAUAGCAUACG)-3'	50	2443	-176	184	1177	752	508	0
5'-r(GCGAAGCCAACG)-3'	67	2432	-167	186	1095	788	532	0
5'-r(GCGCCGCCGGCG)-3'	100	2596	-176	216	1026	949	582	0

Figure S1. Natural logarithm of the observed unfolding equilibrium constant K_{obs} for thermal denaturation of RNA duplexes as a function of glycine betaine molality and temperature. The temperature at a fraction of unfolded duplex of 0.2 is given by filled circles and a fraction of unfolded duplex of 0.8 is given by filled squares. Temperatures in between these two temperatures follow the progression open diamonds > filled diamonds > open circles. A) 5'-r(GAAAUUAUAAAG)-3' at 27.3, 29.2, 31.1, 33.0, and 35.0 $^{\circ}$C; B) 5'-r(GAAAGUAUAAAG)-3' at 34.8, 36.7, 38.6, 40.5, and 42.4 $^{\circ}$C; C) 5'-r(GAAAGUAGAAAC)-3' at 40.4, 42.0, 43.7, 45.3, and 46.9 $^{\circ}$C; D) 5'-r(GAUAGUAGAUAG)-3' at 45.5, 47.1, 48.6, 50.2, and 51.7 $^{\circ}$C; E) 5'-r(GCAAAGUAAACG)-3' at 44.6, 46.1, 47.7, 49.2, and 50.7 $^{\circ}$C; F) 5'-r(GCAAAGCAAACG)-3' at 49.0, 50.1, 51.2, 52.2, and 53.3 $^{\circ}$C; G) 5'-r(GCAUAGCAUACG)-3' at 52.0, 53.3, 54.6, 55.8, and 57.1 $^{\circ}$C; H) 5'-r(GCGAAGCCAACG)-3' at 59.6, 60.8, 62.1, 63.3, and 64.5 $^{\circ}$C; I) 5'-r(GCGCCGCCGGCG)-3' at 80.9, 81.3, 81.6, 82.0, and 82.4 $^{\circ}$C. Linear regression slopes are equal to $-\Delta\mu_{23,4}/RT$. For the 5'-r(GCGCCGCCGGCG)-3' duplex, only the first three data points were used in the regression analysis. Error bars on ln K_{obs} are smaller than symbols.
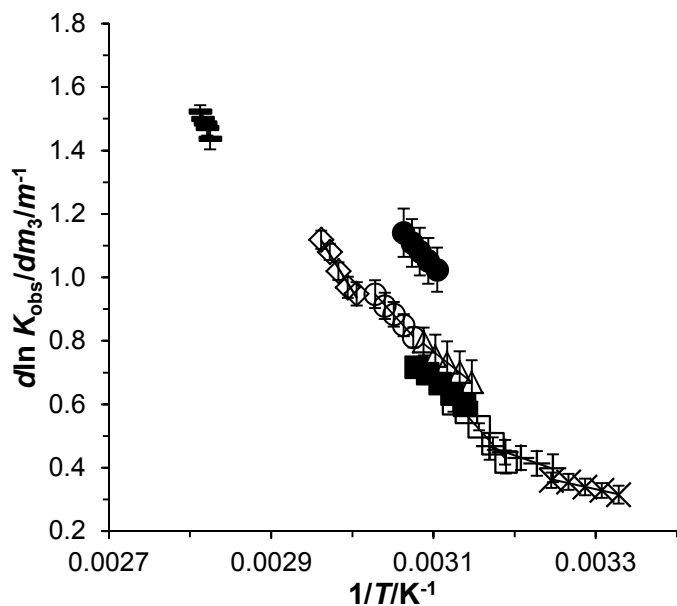
Figure S2. RNA duplex $d\ln K_{obs}/dm_3$ as a function of inverse temperature. 5'-r(GAAAUUAUAAAG)-3' (crosses), 5'-r(GAAAGUAUAAAG)-3' (plus symbols), 5'-r(GAUAGUAGAUAG)-3' (filled squares), 5'-r(GAAAGUAGAAAC)-3' (open squares), 5'-r(GCAAAGUAAACG)-3' (open triangles), 5'-r(GCAAAGCAAACG)-3' (filled circles), 5'-r(GCAUAGCAUACG)-3' (open circles), 5'-r(GCGAAGCCAACG)-3' (open diamonds), 5'-r(GCGCCGCCGGCG)-3' (dash). Slopes from linear regression are equal to $d^2\ln K_{obs}/dm_3d(1/T) = -d\Delta H_{obs}^{o}/dm_3 \times 1/R$.