

## Supporting Material

### The effect of chirality and steric hindrance on intrinsic backbone conformational propensities: Tools for protein design

Matthew Carter Childers, Clare-Louise Towse and Valerie Daggett\*

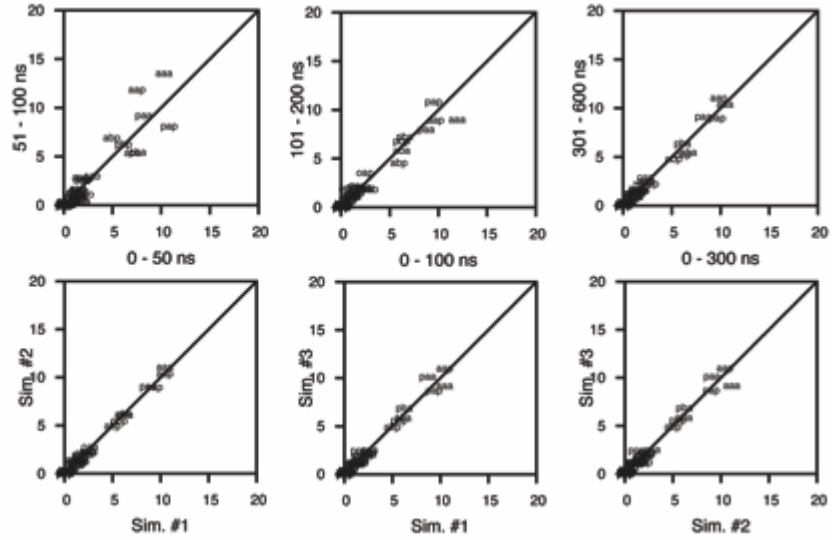
#### Supporting Material Figure Legends

**Figure S1.** Convergence of guest residue sampling across different portions of the trajectories and in replicate simulations under native conditions. Comparison of fraction of time spent in each of the 64 possible conformational states over different portions of the trajectory (above) and across replicate simulations (below) for GGAGG (a), GGGGG (b), and GGWGG (c) in water at 298 K.

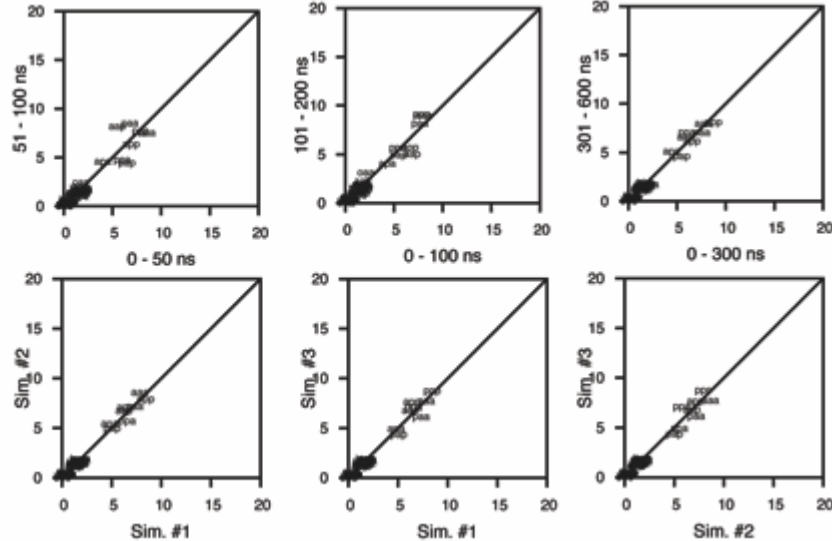
**Figure S2.** Convergence of guest residue sampling across different portions of the trajectories and in replicate simulations under chemically denaturing conditions. Comparison of fraction of time spent in each of the 64 possible conformational states over different portions of the trajectory (above) and across replicate simulations (below) for GGAGG (a), GGGGG (b), and GGWGG (c) in 8M urea at 298 K.

**Figure S3. Intramolecular interactions do not change in response to host peptide sequence or environment.** (A) Hydrogen bond formation in GGAGG, water 298 (left) and in AAAAA, water 298 (right). (B) Hydrophobic interactions in AAAAA, water 298 (left) and in water 498 (right).

**A) GGAGG**  
 $H_2O$ , 298 K



**B) GGGGG**  
 $H_2O$ , 298 K



**C) GGWGG**  
 $H_2O$ , 298 K

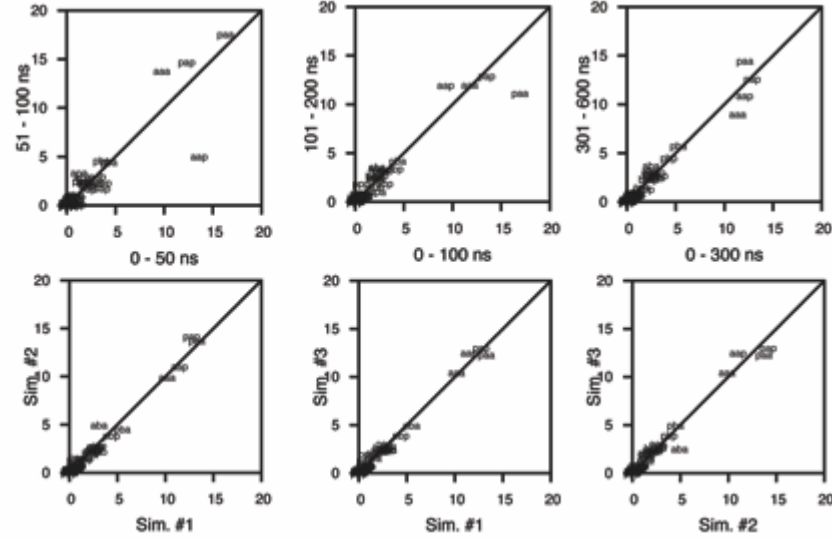
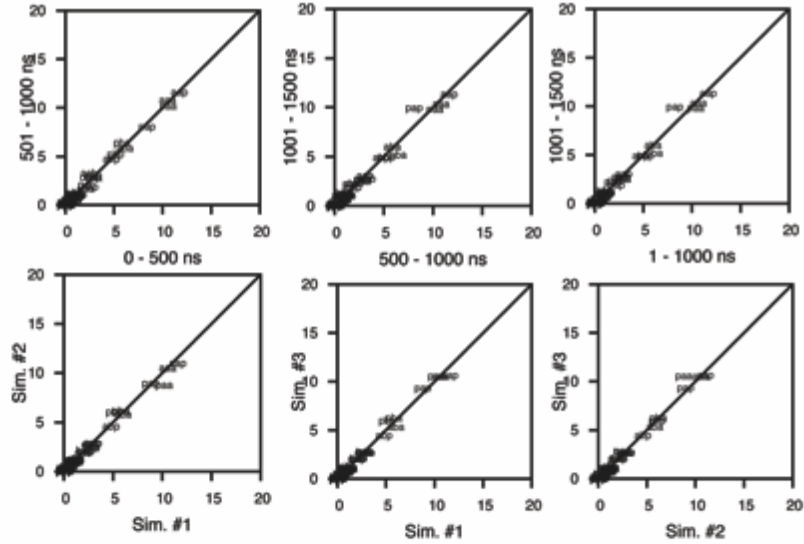
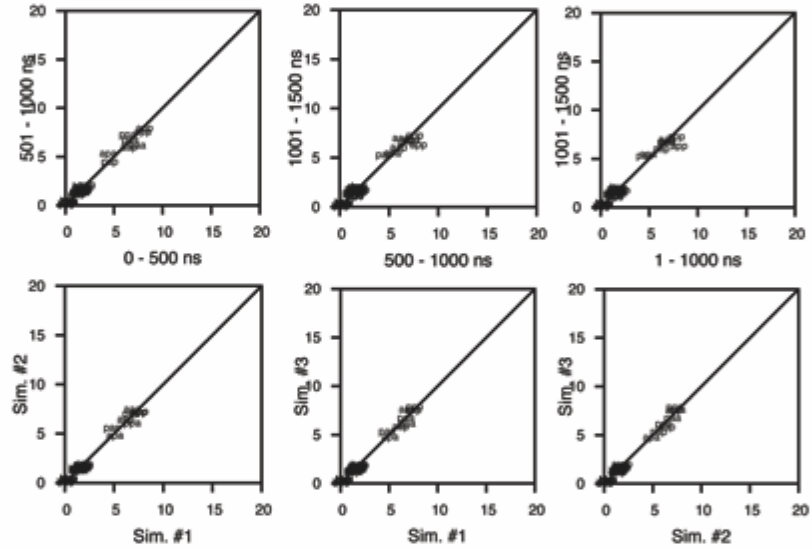


Figure S1

**A) GGAGG**  
8M Urea, 298 K



**B) GGGGG**  
8M Urea, 298 K



**C) GGWGG**  
8M Urea, 298 K

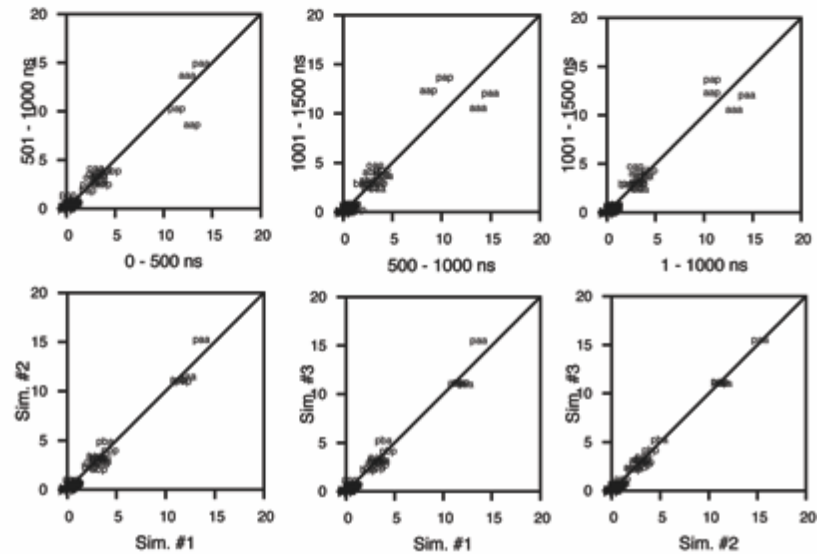
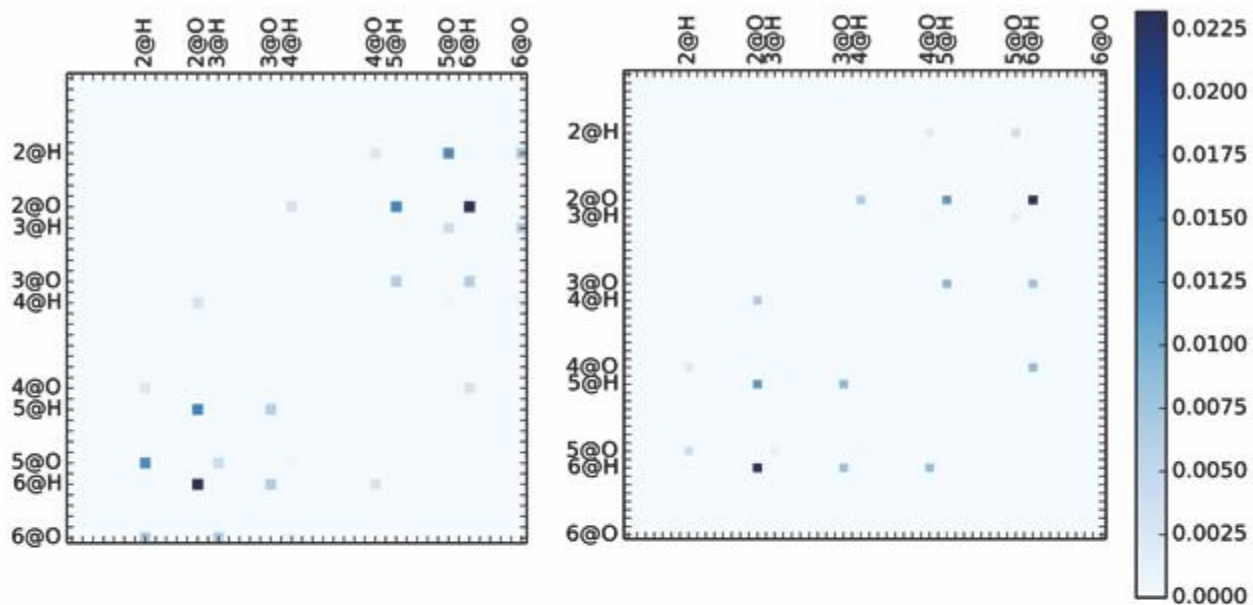


Figure S2

A)



B)

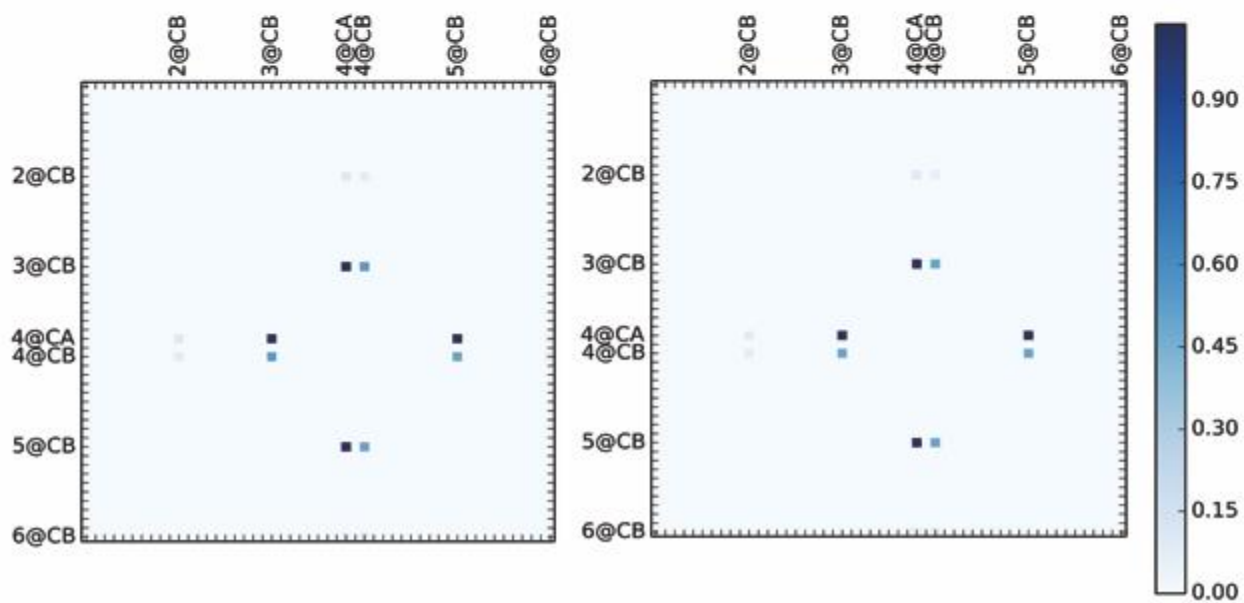


Figure S3

**Table S1. Correlation coefficients (R) between initial and latter portions of the GGXGG trajectories for the 64 conformational states populated by the three central residues.**

<b>Guest X Residue</b>	<b>Water 298 K*</b>	<b>8M Urea 298 K†</b>	<b>Water 498 K§</b>
<b>Ala-1</b>	0.99	1.00	0.99
<b>Ala-2</b>	0.99	0.98	1.00
<b>Ala-3</b>	0.97	0.99	0.99
<b>Arg</b>	0.99	0.99	0.99
<b>Asn</b>	0.99	0.99	1.00
<b>Asp</b>	0.99	0.99	0.99
<b>Ash</b>	0.98	0.99	0.99
<b>Cyh</b>	0.98	0.98	0.99
<b>Gln</b>	0.97	0.97	0.99
<b>Glu</b>	0.99	0.98	1.00
<b>Glh</b>	0.95	0.99	1.00
<b>Gly-1</b>	0.99	0.99	0.99
<b>Gly-2</b>	0.99	0.98	0.95
<b>Gly-3</b>	0.99	0.99	0.98
<b>Hid</b>	0.97	0.99	0.98
<b>Hie</b>	0.99	0.98	0.99
<b>Hip</b>	0.97	0.98	0.99
<b>Ile</b>	0.99	0.98	0.99
<b>Leu</b>	0.99	0.96	0.99
<b>Lys</b>	0.99	0.99	0.99
<b>Met</b>	0.98	0.98	0.99
<b>Phe</b>	1.00	0.99	0.99
<b>Pro</b>	0.98	0.99	0.99
<b>Ser</b>	1.00	0.99	0.99
<b>Thr</b>	0.99	0.97	1.00
<b>Trp-1</b>	0.98	0.98	0.99
<b>Trp-2</b>	0.99	0.96	-
<b>Trp-3</b>	0.99	0.97	-
<b>Tyr</b>	0.97	0.99	0.99
<b>Val</b>	0.99	0.98	0.99
<b>Average</b>	<b>0.99</b>	<b>0.98</b>	<b>1.00</b>

The latter portions were that part of the trajectory (production dynamics) used for analysis. The start position and length of the production dynamics for each set of simulations was defined by the convergence behavior as exhibited in Figure X. \*last 300 ns, †last 500 ns, §last 50 ns.

**Table S2. Conformational propensities of the guest residues (X) in GGXGG in water at 298 K**

Population Frequency (%)												
X	By quadrant				By specific conformational region							
	$Q_{\alpha}$	$Q_{\beta}$	$Q_{\alpha L}$	$Q_{\alpha}$	$\alpha_R$	Near $\alpha_R$	$\alpha_L$	$\beta$	Non- P $\beta$	$P_{III}$	$P_{IR}$	Other
<b>Ala</b>	58.5	32.8	8.2	0.4	23.2	26.8	6.7	19.3	9.3	8.0	6.2	19.6
<b>Ala</b>	56.3	34.6	8.7	0.4	23.3	25.2	7.2	20.9	10.0	8.9	6.6	18.9
<b>Ala</b>	54.9	33.0	11.7	0.4	21.8	25.5	10.0	19.9	9.6	8.4	6.3	18.4
<b>Arg</b>	70.0	24.5	5.4	0.1	30.2	31.7	4.7	17.1	7.9	8.3	2.7	14.6
<b>Asn</b>	77.0	17.9	5.0	0.1	39.6	32.8	4.4	13.6	8.1	4.2	2.7	8.3
<b>Asp</b>	70.7	19.5	9.6	0.1	28.8	38.9	9.1	5.3	3.4	0.4	5.2	14.3
<b>Ash</b>	73.1	19.8	6.9	0.2	35.6	33.6	6.1	15.1	9.6	3.6	3.6	7.9
<b>Cyh</b>	59.2	34.0	6.7	0.1	24.3	27.8	5.8	23.3	10.7	11.1	4.1	16.2
<b>Gln</b>	68.8	28.2	2.9	0.1	30.6	30.3	2.5	20.2	9.2	9.8	3.1	14.5
<b>Glu</b>	60.9	32.8	6.2	0.1	31.0	22.9	5.7	24.5	10.8	12.5	3.0	14.2
<b>Glh</b>	54.4	23.5	21.9	0.2	25.8	22.6	20.0	16.9	7.9	8.0	2.9	12.8
<b>Gly</b>	40.3	9.6	40.4	9.7	15.2	5.6	11.1	6.9	3.3	3.1	1.6	60.0
<b>Gly</b>	41.1	9.1	41.1	8.7	16.1	5.4	11.6	6.6	3.1	3.1	1.4	59.3
<b>Gly</b>	39.2	9.4	42.3	9.1	15.5	5.3	11.8	6.9	3.2	3.2	1.5	59.6
<b>Hid</b>	67.0	25.9	7.0	0.1	26.5	33.4	6.2	19.3	9.4	7.8	3.3	13.4
<b>Hie</b>	70.3	25.9	3.7	0.1	33.2	30.0	3.0	18.6	8.3	10.1	2.1	13.3
<b>Hip</b>	70.1	29.5	0.4	< 0.1	16.9	45.0	0.2	12.8	7.8	2.0	8.9	19.1
<b>Ile</b>	50.8	49.1	0.1	<< 0.1	17.5	24.3	0.1	38.2	13.0	24.8	1.6	18.7
<b>Leu</b>	70.3	23.7	5.9	0.1	35.2	27.7	5.2	20.1	8.2	11.2	1.6	11.0
<b>Lys</b>	71.6	24.3	4.1	< 0.1	31.7	31.3	3.7	17.7	8.3	8.3	2.8	13.8
<b>Met</b>	68.0	26.0	5.9	0.2	31.3	28.7	5.3	19.5	8.6	9.9	2.5	13.7
<b>Phe</b>	68.2	24.5	7.2	0.1	28.4	33.5	6.4	19	9.5	8.3	2.6	11.3
<b>Pro</b>	21.0	79.0	-	-	19.2	<< 0.1	-	73.3	14.4	58.9	-	7.5
<b>Ser</b>	54.9	39.3	5.6	0.2	29.0	17.0	5.0	31.5	11.0	19.7	2.1	16.1
<b>Thr</b>	69.4	29.9	0.7	0.0	41.8	22.7	0.6	22.8	8.7	13.7	0.9	11.5
<b>Trp</b>	70.1	24.1	5.6	0.2	28.7	34.6	5.0	18.2	8.7	8.5	2.5	12.0
<b>Trp</b>	67.2	21.8	10.9	0.1	27.1	34.2	9.8	16.3	7.9	7.4	2.2	11.4
<b>Trp</b>	72.4	19.9	7.4	0.2	30.4	36.1	6.7	12.5	6.9	6.4	2.3	11.2
<b>Tyr</b>	71.4	24.4	4.1	0.1	29.8	35.2	3.6	18.2	9.0	7.9	2.9	11.6
<b>Val</b>	57.5	40.7	1.7	-	21.0	29.9	1.6	29.8	11.0	18.1	1.8	16.5

**Table S3. Conformational propensities of the guest residues (X) in AAXAA in water at 298 K**

Population Frequency (%)												
X	By quadrant				By specific conformational region							
	$Q_{\alpha}$	$Q_{\beta}$	$Q_{\alpha L}$	$Q_{\circ}$	$\alpha_R$	Near $\alpha_R$	$\alpha_L$	$\beta$	Non- P $\beta$	$P_{III}$	$P_{IIR}$	Other
Ala	46.2	39.8	13.6	0.4	20.3	18.1	11.6	28.9	12.8	13.7	6.6	16.9
Ala	41.7	41.8	16.2	0.4	17.7	16.1	14.0	32.2	14.4	15.4	6.1	16.2
Ala	45.6	41.7	12.4	0.3	20.3	17.3	10.4	31.3	13.7	15.2	6.5	16.6
Arg	55.6	33.8	10.3	0.2	26.6	21.7	9.2	28	12.0	14.5	3.4	12.6
Asn	59.2	33.4	7.3	0.1	34.0	21.6	6.3	27.7	16.0	8.7	4.9	8.5
Asp	67.8	21.8	10.3	0.1	29.2	36.2	9.7	6.9	4.6	0.4	6.5	13.5
Ash	65.4	24.5	10.0	0.1	36.5	25.4	9.1	20	12.3	5.4	3.9	7.5
Cyh	48.2	41.4	10.0	0.4	20.8	20.3	8.8	33.2	14.3	17.3	4.3	14.3
Gln	48.2	32.2	19.4	0.2	22.9	18.8	17.7	26.4	11.0	14.1	3.2	12.2
Glu	50.6	36.8	12.4	0.2	25.9	18.1	11.4	28.9	12.7	14.5	4.2	13.2
Glh	51.4	33.9	14.6	0.1	22.7	22.2	13.3	26.4	11.7	13.0	4.2	12.9
Gly	41.2	9.2	39.4	10.2	14.2	3.2	11.5	8	3.7	3.9	1.2	62.4
Hid	62.3	29.6	8.0	0.1	27.3	28.3	7.2	23.1	11.8	9.5	4.0	11.9
Hie	54.6	35.1	10.2	0.1	27.9	20.0	8.9	29.5	13.1	14.9	3.0	12.2
Hip	42.3	27.1	30.1	0.5	8.8	28.2	24.7	16.6	10.3	3.2	8.2	16.6
Ile	39.6	55.7	4.7	<< 0.1	15.5	17.0	4.4	46.1	14.2	31.4	1.8	15.7
Leu	61.1	21.0	17.6	0.3	33.7	21.2	15.8	18	6.9	10.4	1.3	10.7
Lys	55.2	32.1	12.5	0.2	27.2	21.1	11.3	26.3	10.9	14.0	3.3	12.2
Met	51.0	28.7	20.0	0.3	25.3	19.7	18.0	23	10.0	11.7	2.8	12.4
Phe	56.8	25.8	17.2	0.2	26.4	25.1	15.5	20.4	10.5	8.3	3.2	10.9
Pro	5.1	94.9	-	-	3.1	-	-	89.4	11.2	78.2	-	7.6
Ser	45.0	49.9	5.0	0.1	24.0	10.2	4.5	44.6	12.7	31.3	1.7	15.5
Thr	55.0	44.3	0.7	< 0.1	35.77	14.2	0.7	38.1	12.3	25.5	1.2	10.6
Trp	62.3	26.0	11.6	0.2	28.6	28.0	10.5	20.5	10.8	8.1	3.2	10.8
Tyr	54.0	25.7	20.0	0.3	24.0	24.4	18.0	20.1	10.9	7.5	3.7	11.6
Val	42.3	56.5	1.2	<< 0.1	16.8	19.0	1.1	49.4	17.0	31.4	2.3	12.3

**Table S4. Difference in the sampling of conformational regions (%) of GGXGG relative to AAXAA in water at 298 K**

**Population Frequency (%)**

X	By quadrant				By specific conformational region							
	$Q_\alpha$	$Q_\beta$	$Q_{\alpha L}$	$Q_o$	$\alpha_R$	Near $\alpha_R$	$\alpha_L$	$\beta$	Non- P $\beta$	$P_{III}$	$P_{IR}$	Other
Ala	12.3	-6.9	-5.5	0.1	2.9	8.7	-4.9	-9.6	-3.5	-5.6	-0.3	2.7
Arg	14.3	-9.3	-4.9	-0.1	3.6	10.0	-4.5	-10.9	-4.1	-6.2	-0.7	2.0
Asn	17.8	-15.5	-2.3	< 0.1	5.6	11.2	-1.9	-14.1	-8.0	-4.5	-2.2	-0.2
Asp	3.0	-2.3	-0.7	< 0.1	-0.5	2.7	-0.6	-1.6	-1.1	<< 0.1	-1.3	0.8
Ash	7.7	-4.7	-3.1	0.1	-0.9	8.1	-2.9	-4.8	-2.7	-1.8	-0.3	0.4
Cyh	11.0	-7.4	-3.4	-0.2	3.5	7.5	-3.0	-10.0	-3.5	-6.2	-0.2	1.9
Gln	20.7	-4.0	-16.5	-0.1	7.6	11.4	-15.2	-6.2	-1.7	-4.3	-0.2	2.3
Glu	10.3	-4.0	-6.2	-0.1	5.1	4.7	-5.7	-4.4	-1.9	-1.9	-1.2	1.0
Glh	3.0	-10.4	7.3	0.1	3.1	0.4	6.7	-9.5	-3.8	-5.0	-1.3	-0.1
Gly	-0.8	0.4	1.0	-0.5	1.1	2.4	-0.3	-1.1	-0.4	-0.7	0.3	-2.4
Hid	4.7	-3.8	-0.9	< 0.1	-0.8	5.1	-1.0	-4.5	-2.4	-1.7	-0.7	1.5
Hie	15.8	-9.3	-6.5	< 0.1	5.3	10.0	-5.8	-10.2	-4.8	-4.8	-0.9	1.1
Hip	27.7	2.4	-29.7	-0.4	8.1	16.9	-24.5	-3.8	-2.5	-1.2	0.7	2.5
Ile	11.1	-6.6	-4.6	< -0.1	2.0	7.3	-4.3	-7.9	-1.2	-6.6	-0.2	3.0
Leu	9.2	2.8	-11.8	-0.1	1.6	6.5	-10.6	2.1	1.3	0.7	0.3	0.3
Lys	16.4	-7.8	-8.4	-0.1	4.6	10.3	-7.6	-8.7	-2.6	-5.8	-0.5	1.6
Met	17.0	-2.7	-14.2	-0.1	6.0	9.0	-12.8	-3.6	-1.4	-1.9	-0.3	1.3
Phe	11.4	-1.3	-10.0	< -0.1	2.0	8.5	-9.2	-1.4	-1.0	-0.1	-0.6	0.4
Pro	16.0	-16.0	-	-	16.1	<< 0.1	-	-16.1	3.2	-19.3	-	-0.1
Ser	9.9	-10.6	0.6	0.1	5.0	6.8	0.5	-13.2	-1.6	-11.6	0.4	0.6
Thr	14.4	-14.4	0.0	0.0	6.0	8.5	-0.1	-15.3	-3.4	-11.8	-0.3	1.0
Trp	7.8	-1.9	-5.9	<< 0.1	0.1	6.6	-5.5	-2.2	-2.1	0.4	-0.7	1.2
Tyr	17.3	-1.3	-15.9	-0.2	5.8	10.8	-14.4	-2.0	-1.8	0.4	-0.8	< 0.1
Val	15.3	-15.8	0.5	<< -0.1	4.1	10.8	0.5	-19.7	-6.0	-13.3	-0.5	4.3



**Table S5. Similarity correlation matrices for the  $\phi/\psi$  frequency distributions of the guest residues in the GGXGG and AAXAA peptides in water at 298 K.**

		GGXGG water 298 K																									
		ALA	ARG	ASH	ASN	ASP	CYS	GLH	GLN	GLU	GLY	HID	HIE	HIP	ILE	LEU	LYS	MET	PHE	PRO	SER	THR	TRP	TYR	VAL		
AAXAA water 298 K	ALA		0.94	0.93	0.92	0.87	0.96	0.90	0.95	0.94	<b>0.43</b>	0.95	0.95	0.85	0.69	0.92	0.94	0.94	0.95	<b>0.21</b>	0.87	0.87	0.95	0.95	0.83	ALA	
	ARG	0.95		0.94	0.95	0.84	0.98	0.91	1.00	0.97	<b>0.41</b>	0.99	0.99	0.80	0.70	0.98	1.00	1.00	0.99	<b>0.15</b>	0.87	0.90	0.99	0.99	0.87	ARG	
	ASH	0.87	0.91		0.99	0.82	0.91	0.87	0.94	0.93	<b>0.40</b>	0.95	0.96	0.78	0.54	0.94	0.94	0.94	0.96	<b>0.15</b>	0.84	0.90	0.95	0.96	0.73	ASH	
	ASN	0.88	0.92	0.99		0.79	0.91	0.87	0.95	0.94	<b>0.42</b>	0.95	0.97	0.75	0.56	0.96	0.95	0.95	0.96	<b>0.16</b>	0.84	0.91	0.95	0.96	0.74	ASN	
	ASP	0.80	0.83	0.78	0.76		0.89	0.80	0.83	0.81	<b>0.27</b>	0.86	0.85	0.78	0.65	0.78	0.82	0.82	0.85	<b>0.03</b>	0.77	0.82	0.87	0.86	0.79	ASP	
	CYS	0.96	0.98	0.85	0.87	0.83		0.91	0.98	0.97	<b>0.37</b>	0.98	0.97	0.82	0.78	0.95	0.97	0.97	0.97	<b>0.21</b>	0.91	0.91	0.98	0.97	0.91	CYS	
	GLH	0.96	0.98	0.89	0.89	0.83	0.97		0.89	0.92	<b>0.49</b>	0.91	0.89	0.68	0.61	0.91	0.90	0.92	0.91	<b>0.16</b>	0.84	0.83	0.90	0.89	0.77	GLH	
	GLN	0.96	0.96	0.86	0.87	0.79	0.95	0.99		0.98	<b>0.41</b>	0.99	0.99	0.80	0.72	0.98	1.00	0.99	0.99	<b>0.18</b>	0.89	0.92	0.99	0.99	0.87	GLN	
	GLU	0.96	0.98	0.91	0.93	0.78	0.96	0.98	0.97		<b>0.46</b>	0.95	0.98	0.72	0.72	0.98	0.97	0.98	0.96	<b>0.27</b>	0.94	0.95	0.96	0.95	0.86	GLU	
	GLY	<b>0.38</b>	<b>0.35</b>	<b>0.33</b>	<b>0.33</b>	<b>0.20</b>	<b>0.31</b>	<b>0.37</b>	<b>0.40</b>	<b>0.40</b>		<b>0.39</b>	<b>0.42</b>	<b>0.22</b>	<b>0.19</b>	<b>0.44</b>	<b>0.42</b>	<b>0.43</b>	<b>0.39</b>	<b>0.11</b>	<b>0.40</b>	<b>0.39</b>	<b>0.38</b>	<b>0.37</b>	<b>0.26</b>	GLY	
	HID	0.92	0.98	0.93	0.94	0.86	0.94	0.96	0.92	0.95	<b>0.31</b>		0.98	0.84	0.68	0.97	0.99	0.98	1.00	<b>0.14</b>	0.85	0.88	1.00	0.99	0.86	HID	
	HIE	0.96	0.99	0.93	0.95	0.81	0.97	0.97	0.95	0.98	<b>0.37</b>	0.96		0.78	0.71	0.98	0.98	0.99	0.98	<b>0.21</b>	0.91	0.95	0.98	0.98	0.87	HIE	
	HIP	0.73	0.67	0.59	0.57	0.68	0.68	0.77	0.75	0.67	<b>0.38</b>	0.69	0.64		0.56	0.70	0.79	0.76	0.82	<b>0.02</b>	0.60	0.63	0.82	0.82	0.72	HIP	
	ILE	0.73	0.73	<b>0.48</b>	0.52	0.52	0.80	0.70	0.69	0.69	<b>0.18</b>	0.64	0.72	<b>0.40</b>		0.67	0.69	0.70	0.67	<b>0.30</b>	0.78	0.72	0.69	0.68	0.95	ILE	
	LEU	0.92	0.97	0.94	0.93	0.80	0.92	0.96	0.96	0.96	<b>0.41</b>	0.95	0.97	0.65	0.61		0.99	0.99	0.98	<b>0.21</b>	0.90	0.93	0.97	0.97	0.83	LEU	
	LYS	0.95	0.99	0.92	0.93	0.81	0.97	0.99	0.97	0.99	<b>0.37</b>	0.97	0.99	0.67	0.70	0.98		1.00	0.99	<b>0.15</b>	0.87	0.90	0.99	0.99	0.85	LYS	
	MET	0.95	0.97	0.89	0.89	0.80	0.94	0.98	0.99	0.97	<b>0.40</b>	0.94	0.96	0.74	0.64	0.98	0.98		0.99	<b>0.18</b>	0.89	0.92	0.99	0.99	0.86	MET	
	PHE	0.93	0.97	0.94	0.93	0.84	0.93	0.98	0.97	0.96	<b>0.36</b>	0.97	0.96	0.75	0.60	0.98	0.98	0.98		<b>0.15</b>	0.86	0.89	1.00	1.00	0.84	PHE	
	PRO	<b>0.30</b>	<b>0.19</b>	<b>0.08</b>	<b>0.13</b>	<b>-0.02</b>	<b>0.29</b>	<b>0.18</b>	<b>0.20</b>	<b>0.22</b>	<b>0.06</b>	<b>0.10</b>	<b>0.25</b>	<b>-0.01</b>	<b>0.49</b>	<b>0.12</b>	<b>0.19</b>	<b>0.15</b>	<b>0.09</b>		<b>0.45</b>	<b>0.30</b>	<b>0.14</b>	<b>0.14</b>	<b>0.25</b>	PRO	
	SER	0.81	0.78	0.63	0.67	0.54	0.84	0.74	0.75	0.77	<b>0.30</b>	0.68	0.81	<b>0.34</b>	0.86	0.71	0.77	0.71	0.66	0.61		0.95	0.86	0.86	0.85	SER	
	THR	0.84	0.87	0.82	0.85	0.69	0.88	0.81	0.80	0.87	<b>0.30</b>	0.81	0.91	<b>0.36</b>	0.75	0.83	0.86	0.79	0.78	<b>0.42</b>	0.90		0.89	0.90	0.84	THR	
	TRP	0.93	0.98	0.94	0.94	0.88	0.94	0.97	0.94	0.95	<b>0.33</b>	0.99	0.97	0.71	0.62	0.97	0.98	0.96	0.99	<b>0.09</b>	0.67	0.80		1.00	0.86	TRP	
	TYR	0.93	0.96	0.91	0.90	0.84	0.93	0.98	0.97	0.95	<b>0.37</b>	0.96	0.94	0.79	0.59	0.97	0.96	0.98	0.99	<b>0.07</b>	0.63	0.74	0.98		0.85	TYR	
	VAL	0.79	0.81	0.58	0.63	0.59	0.86	0.77	0.75	0.76	<b>0.18</b>	0.73	0.80	<b>0.43</b>	0.98	0.68	0.78	0.70	0.67	<b>0.48</b>	0.88	0.82	0.71	0.66		VAL	
		ALA	ARG	ASH	ASN	ASP	CYS	GLH	GLN	GLU	GLY	HID	HIE	HIP	ILE	LEU	LYS	MET	PHE	PRO	SER	THR	TRP	TYR	VAL		

**Table S6. Conformational propensities of the guest residues (X) in GGXGG in urea at 298 K.**

**Population Frequency (%)**

X	By quadrant				By specific conformational region							
	Q <sub>α</sub>	Q <sub>β</sub>	Q <sub>αL</sub>	Q <sub>o</sub>	α <sub>R</sub>	Near α <sub>R</sub>	α <sub>L</sub>	β	Non-P β	P <sub>III</sub>	P <sub>IR</sub>	Other
Ala	63.8	30.7	5.1	0.4	20.3	34.7	3.9	19.4	9.1	8.5	5.5	18.2
Ala	64.8	31.5	3.4	0.3	20.3	35.9	2.5	19.6	9.1	8.7	5.5	18.1
Ala	61.7	31.4	6.6	0.3	19.4	33.9	5.2	20.2	9.3	9.0	5.6	17.6
Arg	67.6	27.9	4.4	0.1	23.6	36.3	3.8	22.0	10.0	11.0	2.6	12.6
Asn	78.9	19.2	1.8	0.1	33.4	40.7	1.5	15.5	8.7	5.5	2.5	7.6
Asp	81.5	16.5	1.9	0.1	24.8	53.4	1.6	5.2	3.4	0.4	4.3	12.1
Ash	73.6	18.3	8.0	0.1	28.8	41.0	7.1	14.3	8.8	3.9	3.0	7.5
Cyh	66.1	29.4	4.3	0.2	20.9	38.1	3.7	21.7	9.6	11.2	2.6	14.0
Gln	74.6	22.8	2.6	< 0.1	27.8	38.9	2.2	17.1	7.9	8.3	2.2	12.8
Glu	64.3	31.0	4.6	0.1	27.9	28.9	4.1	25.3	10.4	14.1	2.1	12.7
Glh	73.0	24.3	2.7	< 0.1	23.8	41.4	2.3	16.5	8.0	7.3	3.2	14.0
Gly	39.9	10.4	39.9	9.8	12.6	8.0	8.4	7.6	3.7	3.4	1.6	62.2
Gly	41.3	9.3	39.7	9.7	13.0	8.4	7.8	6.7	3.2	3.0	1.6	63.1
Gly	39.9	10.0	40.8	9.4	12.0	8.2	8.3	7.3	3.5	3.3	1.6	63.1
Hid	73.8	21.7	4.3	0.1	24.4	42.3	3.8	15.6	7.6	7.0	2.4	12.5
Hie	70.1	23.5	6.1	0.2	25.1	38.0	5.2	18.2	7.2	10.3	1.7	12.6
Hip	75.1	23.1	1.8	0.1	13.0	54.7	1.5	9.4	5.8	1.5	6.6	16.9
Ile	58.3	41.6	0.2	<< 0.1	13.3	36.3	0.2	29.9	10.6	18.8	1.3	19.5
Leu	77.2	19.0	3.7	0.1	32.0	37.4	3.3	16.4	6.5	9.4	1.1	10.2
Lys	73.3	23.2	3.5	0.1	27.1	38.5	3.1	17.7	8.2	8.5	2.4	12.2
Met	67.4	22.3	10.1	0.2	24.1	36.3	9.2	17.1	7.3	8.9	2.1	12.2
Phe	76.3	21.4	2.2	0.1	27.2	42.9	2.0	16.8	8.5	7.3	2.2	10.0
Pro	7.2	92.8	-	-	5.2	<< 0.1	-	86.1	16.1	70.0	-	8.7
Ser	55.5	41.7	2.7	0.1	26.2	20.2	2.4	35.7	11.1	24.1	1.5	14.5
Thr	62.0	38.0	< 0.1	<< 0.1	33.8	23.4	< 0.1	31.3	10.8	20.3	0.6	11.1
Trp	76.6	21.4	1.9	0.1	27.6	42.4	1.6	16.4	8.4	7.0	2.1	10.8
Trp	75.5	19.1	5.4	0.1	26.7	42.5	4.7	14.4	6.9	6.6	1.9	10.7
Trp	73.7	20.3	5.8	0.2	25.5	41.9	5.2	15.7	7.6	7.1	2.2	10.6
Tyr	77.0	18.2	4.7	0.1	28.4	42.7	3.9	13.8	6.9	6.0	1.9	10.2
Val	65.2	34.7	< 0.1	<< 0.1	20.5	38.0	< 0.1	25.4	9.6	15.3	1.7	14.9

**Table S7. Conformational propensities of the guest residues (X) in AAXAA in urea at 298 K**

**Population Frequency (%)**

X	By quadrant				By specific conformational region							
	Q <sub>α</sub>	Q <sub>β</sub>	Q <sub>αL</sub>	Q <sub>o</sub>	α <sub>R</sub>	Near α <sub>R</sub>	α <sub>L</sub>	β	Non-P β	PIIL	PIR	Other
Ala	45.1	48.1	6.7	0.2	13.1	23.6	5.3	39.7	18.2	17.6	8.1	14.0
Ala	50.4	40.4	8.8	0.3	16.2	26.3	7.0	32.7	13.8	16.3	5.9	14.6
Ala	40.6	48.5	10.6	0.3	13.6	19.3	8.9	39	16.5	19.0	8.3	14.4
Arg	55.8	37.9	6.2	0.1	19.2	29.7	5.7	33.2	14.6	16.8	3.6	10.4
Asn	50.9	44.7	4.3	< 0.1	20.1	27.2	3.7	37.8	20.9	12.5	7.2	8.3
Asp	81.7	15.8	2.4	< 0.1	23.7	55.5	2.2	5.4	3.4	0.3	4.7	10.3
Ash	57.9	34.5	7.6	0.1	25.0	29.7	6.8	28	16.5	5.8	8.9	7.2
Cyh	44.0	50.9	5.0	0.1	13.0	22.7	4.2	44.4	19.7	21.9	6.1	12.4
Gln	58.8	32.8	8.3	0.1	21.9	29.5	7.5	28.8	12.2	15.0	3.3	10.7
Glu	53.6	42.9	3.4	0.1	22.0	23.7	3.0	38.6	15.6	21.3	3.4	11.1
Glh	48.3	36.2	15.4	0.2	15.9	25.2	13.5	31.2	13.5	15.6	4.5	11.9
Gly	35.2	12.1	39.1	13.5	8.5	3.7	9.8	11.3	5.4	5.0	1.9	65.7
Gly	37.8	12.3	38.4	11.5	9.5	4.7	8.9	11.5	5.3	5.5	1.6	64.6
Gly	39.8	11.1	36.8	12.4	9.3	4.6	8.7	10.4	5.1	4.5	1.9	66.0
Hid	75.9	19.8	4.1	0.2	25.1	44.2	3.5	15.4	8.1	6.1	2.6	10.4
Hie	53.7	42.1	4.2	< 0.1	16.9	29.1	3.5	37.4	17.4	17.6	4.3	11.1
Hip	63.3	14.7	21.5	0.5	10.0	47.7	16.6	8.6	4.7	2.1	4.4	14.5
Ile	29.6	67.6	2.9	< 0.1	6.8	15.6	2.6	64.2	23.5	39.8	1.7	10.0
Leu	55.1	36.8	7.8	0.3	22.9	25.7	6.9	33.3	13.5	18.2	3.1	9.8
Lys	53.5	39.7	6.7	< 0.1	19.2	27.2	6.0	35.3	14.5	18.7	4.3	10.1
Met	60.6	34.8	4.5	0.1	21.9	31.5	4.0	30.4	12.6	16.1	3.5	10.4
Phe	60.1	35.9	3.9	< 0.1	20.2	34.5	3.4	30.1	16.3	10.4	6.2	9.0
Pro	7.1	92.9	-	-	5.0	-	-	86.9	10.3	76.6	-	8.1
Ser	49.0	45.0	5.7	0.3	23.5	15.4	4.9	41.8	10.3	31.2	0.9	13.7
Thr	71.3	28.6	0.1	< 0.1	42.1	24.2	0.1	24.9	7.1	17.6	0.6	8.4
Trp	64.2	20.5	15.0	0.3	19.4	38.9	13.1	16.7	9.3	5.9	2.9	10.5
Trp	63.2	30.0	6.6	0.2	22.0	35.0	5.6	25.3	14.3	8.6	4.5	10.0
Trp	60.9	29.8	9.1	0.2	22.0	33.3	7.9	25.3	13.3	9.4	4.6	9.4
Tyr	76.3	22.8	0.9	< 0.1	25.8	44.2	0.8	18	10.4	5.7	3.9	9.2
Val	51.5	46.6	1.8	< 0.1	16.1	29.3	1.7	42.4	16.8	24.7	1.8	9.6

**Table S8. Difference in the sampling of conformational regions of GGXGG relative to AAXAA in urea at 298 K**

Population Frequency (%)												
X	By quadrant				By specific conformational region							
	Q <sub>α</sub>	Q <sub>β</sub>	Q <sub>αL</sub>	Q <sub>o</sub>	α <sub>R</sub>	Near α <sub>R</sub>	α <sub>L</sub>	β	Non-P β	P <sub>IIL</sub>	P <sub>IR</sub>	Other
Ala	18.7	-17.4	-1.5	0.2	7.2	11.2	-1.5	-20.3	-9.2	-9.2	-2.7	4.2
Arg	11.8	-10.0	-1.8	0.1	4.4	6.7	-1.8	-11.1	-4.6	-5.9	-1.0	2.2
Asn	28.0	-25.5	-2.6	<0.1	13.3	13.4	-2.2	-22.3	-12.2	-7.0	-4.6	-0.7
Asp	-0.2	0.7	-0.5	0.1	1.1	-2.1	-0.6	-0.2	<<0.1	0.1	-0.4	1.8
Ash	15.9	-16.2	0.3	0.1	3.8	11.3	0.3	-13.7	-7.7	-1.9	-5.9	0.3
Cyh	21.9	-21.2	-0.7	0.1	7.8	15.4	-0.5	-22.7	-10.1	-10.7	-3.5	1.6
Gln	16.0	-10.0	-5.9	-0.1	5.9	9.4	-5.3	-11.7	-4.3	-6.7	-1.1	2.1
Glu	10.7	-12.0	1.3	<<-0.1	5.9	5.2	1.1	-13.4	-5.2	-7.3	-1.3	1.6
Glh	24.9	-12.0	-12.7	-0.1	7.9	16.2	-11.2	-14.7	-5.5	-8.2	-1.3	2.2
Gly	4.6	-1.7	0.7	-3.7	4.2	4.3	-1.4	-3.7	-1.7	-1.6	-0.4	-3.5
Hid	-2.1	1.9	0.2	<-0.1	-0.7	-1.9	0.3	0.2	-0.6	1.0	-0.2	2.2
Hie	16.3	-18.4	1.9	0.2	8.1	8.8	1.7	-19.2	-10.3	-7.3	-2.6	1.4
Hip	11.8	8.4	-19.7	-0.4	3.0	7.0	-15.1	0.9	1.1	-0.6	2.2	2.4
Ile	28.8	-26.1	-2.7	<<-0.1	6.5	20.7	-2.4	-34.3	-12.9	-21.0	-0.4	9.5
Leu	22.1	-17.9	-4.0	-0.2	9.1	11.8	-3.5	-16.9	-7.0	-8.8	-1.9	0.4
Lys	19.9	-16.8	-3.2	0.1	7.9	11.3	-2.9	-17.6	-6.2	-10.2	-1.9	2.2
Met	6.6	-12.4	5.6	0.2	2.1	4.8	5.2	-13.3	-5.3	-7.2	-1.4	1.7
Phe	16.2	-14.5	-1.7	<0.1	7.0	8.3	-1.4	-13.4	-7.8	-3.1	-4.0	1.0
Pro	0.2	-0.2	-	-	0.3	<<0.1	-	-0.9	5.8	-6.7	-	0.6
Ser	6.7	-3.5	-3.0	-0.2	2.6	4.7	-2.5	-6.1	0.8	-7.0	0.6	0.8
Thr	-9.3	9.4	<0.1	<<0.1	-8.3	-0.8	<-0.1	6.4	3.7	2.7	<0.1	2.7
Trp	12.5	0.9	-13.1	-0.2	8.2	3.6	-11.5	-0.3	-0.9	1.1	-0.8	0.3
Tyr	0.5	-4.4	3.8	0.1	2.6	-1.6	3.2	-4.2	-3.5	0.3	-2.0	1.0
Val	13.7	-11.9	-1.8	<<-0.1	4.4	8.6	-1.7	-17.0	-7.2	-9.4	-0.1	5.3

**Table S9. Conformational propensities of the guest residues (X) in GGXGG in water at 498 K.**

Population Frequency (%)												
X	By quadrant				By specific conformational region							
	Q <sub>α</sub>	Q <sub>β</sub>	Q <sub>αL</sub>	Q <sub>o</sub>	α <sub>R</sub>	Near α <sub>R</sub>	α <sub>L</sub>	β	Non- P β	PIIL	PIR	Other
<b>Ala</b>	44.0	46.5	8.0	1.5	14.7	17.2	4.5	29.5	17.7	9.0	7.5	29.4
<b>Ala</b>	42.1	47.6	8.6	1.7	14.2	16.2	5.0	30.4	18.2	9.4	7.6	29.4
<b>Ala</b>	44.1	45.2	9.1	1.6	15.2	17.1	5.4	28.3	16.5	9.1	7.2	29.4
<b>Arg</b>	49.3	44.7	5.5	0.5	20.0	19.0	4.0	30.2	17.2	10.9	5.2	23.8
<b>Asn</b>	51.4	42.3	5.5	0.8	22.2	20.6	3.7	31.1	18.6	9.9	5.3	19.8
<b>Asp</b>	49.7	38.2	11.2	0.9	19.2	25.0	8.4	17.1	10.8	3.2	8.3	25.0
<b>Ash</b>	51.4	41.0	6.8	0.8	21.6	23.2	4.3	28.2	18.5	6.3	7.1	19.0
<b>Cyh</b>	45.1	48.2	5.9	0.8	17.6	17.2	4.2	32.4	18.1	12.3	5.4	25.2
<b>Gln</b>	48.8	44.7	5.7	0.8	20.0	18.6	4.1	30.5	17.5	10.8	5.3	23.7
<b>Glu</b>	45.7	48.3	5.6	0.4	19.9	15.9	4.1	33.8	18.2	13.6	5.1	23.3
<b>Glh</b>	47.4	44.4	7.2	0.9	18.0	19.8	5.4	29.3	17.5	9.3	6.2	23.9
<b>Gly</b>	31.5	17.9	33.0	17.6	8.6	5.2	5.4	11.6	7.1	3.5	3.0	67.3
<b>Hid</b>	50.1	43.2	6.0	0.7	19.4	20.8	4.2	29.5	17.5	9.6	5.7	22.9
<b>Hie</b>	49.9	44.8	4.5	0.7	21.8	17.1	3.0	33.7	18.1	14.1	3.4	22.6
<b>Hip</b>	46.4	45.2	7.8	0.7	12.5	24.6	5.4	25.6	17.3	4.7	9.5	26.0
<b>Ile</b>	41.3	57.9	0.8	< 0.1	17.0	15.5	0.6	43.0	20.8	21.0	3.0	22.0
<b>Leu</b>	54.9	40.7	4.0	0.4	25.3	19.5	2.9	30.3	16.7	11.7	3.9	19.9
<b>Lys</b>	52.3	43.0	4.2	0.5	21.4	20.1	3.0	29.5	17.1	10.3	5.1	23.0
<b>Met</b>	52.0	41.3	6.0	0.7	22.3	19.2	4.5	28.6	16.0	10.7	4.4	23.0
<b>Phe</b>	49.4	44.8	5.2	0.6	20.3	20.3	3.7	32.9	18.7	12.1	4.6	20.4
<b>Pro</b>	21.9	78.1	-	-	17.7	< 0.1	-	68.0	19.8	48.3	<< 0.1	14.3
<b>Ser</b>	47.1	47.2	4.7	0.9	21.3	13.7	3.5	33.2	16.4	15.3	3.8	26.0
<b>Thr</b>	48.8	49.9	1.2	0.1	25.4	14.1	1.0	36.6	17.4	18.1	2.7	21.3
<b>Trp</b>	47.6	46.5	5.2	0.6	19.6	18.7	3.7	34.0	19.1	12.8	4.7	21.4
<b>Tyr</b>	49.6	44.7	5.2	0.6	20.5	20.5	3.6	32.5	18.7	11.6	4.8	20.3
<b>Val</b>	42.7	55.3	1.8	0.2	17.7	17.1	1.5	40.5	20.6	18.4	3.6	21.1

**Table S10. Conformational propensities of the guest residues (X) in AAXAA in water at 498 K**

**Population Frequency (%)**

X	By quadrant				By specific conformational region							
	Q <sub>α</sub>	Q <sub>β</sub>	Q <sub>αL</sub>	Q <sub>o</sub>	α <sub>R</sub>	Near α <sub>R</sub>	α <sub>L</sub>	β	Non-P β	P <sub>III</sub>	P <sub>III</sub>	Other
Ala	41.0	48.7	8.5	1.9	15.7	14.0	5.1	33.6	19.8	10.6	6.9	27.9
Ala	41.9	48.4	8.2	1.4	15.8	14.1	5.1	33.5	20.3	10.1	7.0	27.5
Ala	40.1	49.3	8.9	1.7	15.0	13.6	5.4	34.8	20.6	10.3	7.1	28.0
Arg	44.2	48.9	6.0	0.9	19.4	15.7	4.6	34.4	19.9	12.1	5.5	22.7
Asn	45.0	47.0	7.3	0.7	21.5	15.9	5.0	36.6	22.5	11.1	5.5	18.4
Asp	48.5	37.1	13.3	1.1	20.4	23.0	10.3	15.1	9.8	2.4	8.2	25.9
Ash	49.0	40.9	9.0	1.1	23.0	19.5	6.5	29.2	19.3	6.1	7.2	18.5
Cyh	43.2	51.2	5.1	0.6	18.4	14.4	3.5	36.1	20.6	13.3	5.1	24.6
Gln	44.6	46.1	8.5	0.8	20.1	15.4	6.4	32.3	18.7	11.3	5.1	22.9
Glu	40.8	50.7	8.0	0.5	19.3	12.4	6.4	35.8	20.1	13.4	5.4	23.1
Glh	43.2	48.9	7.2	0.7	17.7	16.2	5.4	33.4	20.0	10.7	6.4	23.6
Gly	31.5	17.1	32.0	19.4	9.2	4.2	6.0	11.5	7.2	3.3	2.7	67.4
Hid	42.4	47.2	9.4	1.0	17.4	16.4	6.9	33	20.0	10.2	6.0	23.2
Hie	44.3	48.9	6.1	0.7	22.4	13.5	3.0	36.1	19.2	15.4	3.3	23.3
Hip	47.2	46.6	5.6	0.5	14.5	23.0	3.7	28.4	19.4	4.9	9.6	24.8
Ile	39.2	59.7	1.0	0.1	17.3	13.2	0.8	45	21.9	21.9	2.9	22.0
Leu	52.2	39.9	6.8	1.1	26.0	16.7	5.1	29.9	16.7	11.3	3.8	20.3
Lys	47.1	45.5	6.6	0.9	21.4	16.0	5.0	32.2	18.6	11.3	4.9	22.7
Met	47.6	44.4	6.7	1.3	22.0	16.0	5.1	31.3	17.9	11.4	4.7	22.9
Phe	45.0	49.0	5.5	0.5	19.9	16.5	4.1	36.5	21.3	12.8	5.0	20.5
Pro	23.5	76.5	< 0.1	-	19.1	<< 0.1	-	67.1	18.7	48.5	<< 0.1	13.7
Ser	43.9	51.2	4.2	0.8	21.8	10.0	3.2	37	17.9	17.5	3.8	25.7
Thr	48.6	50.2	1.1	0.1	28.1	11.1	0.9	37.3	17.6	18.8	2.4	21.2
Trp	44.4	47.9	6.9	0.8	20.2	15.2	5.3	35.3	20.0	13.4	4.1	21.9
Tyr	48.7	43.2	7.1	1.0	22.3	17.8	5.4	30.9	18.0	10.7	4.5	21.2
Val	33.9	63.1	3.0	< 0.1	15.4	11.2	2.5	49.9	24.8	23.5	3.5	19.1

**Table S11. Difference in the sampling of conformational regions of GGXGG relative to AAXAA in water at 498 K**

**Population Frequency (%)**

X	By quadrant				By specific conformational region							
	Q <sub>α</sub>	Q <sub>β</sub>	Q <sub>αL</sub>	Q <sub>o</sub>	α <sub>R</sub>	Near α <sub>R</sub>	α <sub>L</sub>	β	Non-P β	P <sub>III</sub>	P <sub>IR</sub>	Other
<b>Ala</b>	3.0	-2.2	-0.5	-0.4	-1	3.2	-0.6	-4.1	-2.1	-1.6	0.6	1.5
<b>Arg</b>	5.1	-4.1	-0.5	-0.5	0.6	3.3	-0.6	-4.2	-2.8	-1.2	-0.3	1.1
<b>Asn</b>	6.5	-4.7	-1.7	< 0.1	0.6	4.7	-1.3	-5.5	-4.0	-1.3	-0.2	1.4
<b>Asp</b>	1.2	1.1	-2.1	-0.2	-1.1	2.0	-1.9	2.0	1.1	0.8	0.1	-0.9
<b>Ash</b>	2.4	0.1	-2.2	-0.2	-1.4	3.7	-2.1	-1.0	-0.7	0.1	< -0.1	0.5
<b>Cyh</b>	1.9	-3.0	0.8	0.2	-0.8	2.8	0.6	-3.7	-2.6	-1.0	0.4	0.6
<b>Gln</b>	4.2	-1.5	-2.8	< 0.1	-0.1	3.1	-2.3	-1.8	-1.2	-0.5	0.1	0.8
<b>Glu</b>	5.0	-2.4	-2.4	-0.1	0.6	3.5	-2.3	-2.0	-2.0	0.2	-0.2	0.2
<b>Glh</b>	4.2	-4.4	0.1	0.2	0.3	3.5	-0.1	-4.1	-2.5	-1.4	-0.2	0.3
<b>Gly</b>	< -0.1	0.8	1.0	-1.7	-0.6	0.9	-0.6	0.1	-0.1	0.2	0.3	-0.1
<b>Hid</b>	7.7	-4.0	-3.4	-0.3	2.0	4.5	-2.7	-3.4	-2.5	-0.6	-0.3	-0.3
<b>Hie</b>	2.6	-2.9	0.4	-0.1	-0.6	3.6	< 0.1	-2.4	-1.1	-1.3	0.1	-0.7
<b>Hip</b>	-0.9	-1.5	2.2	0.1	-2.0	1.6	1.7	-2.8	-2.2	-0.2	-0.1	1.2
<b>Ile</b>	2.1	-1.8	-0.2	-0.1	-0.4	2.4	-0.2	-2.0	-1.1	-0.8	0.1	<< -0.1
<b>Leu</b>	2.6	0.8	-2.8	-0.7	-0.7	2.7	-2.2	0.4	< 0.1	0.4	0.1	-0.4
<b>Lys</b>	5.2	-2.5	-2.4	-0.4	< 0.1	4.1	-1.9	-2.6	-1.5	-1.1	0.2	0.3
<b>Met</b>	4.4	-3.1	-0.7	-0.6	0.3	3.2	-0.7	-2.7	-1.9	-0.7	-0.3	< 0.1
<b>Phe</b>	4.5	-4.2	-0.3	0.1	0.4	3.8	-0.4	-3.6	-2.5	-0.7	-0.4	-0.1
<b>Pro</b>	-1.6	1.6	<< -0.1	-	-1.4	<< 0.1	-	0.9	1.1	-0.2	< -0.1	0.6
<b>Ser</b>	3.3	-3.9	0.5	0.1	-0.5	3.7	0.3	-3.9	-1.6	-2.2	< -0.1	0.3
<b>Thr</b>	0.2	-0.3	0.1	0.0	-2.7	3.0	0.1	-0.7	-0.2	-0.6	0.3	0.1
<b>Trp</b>	3.3	-1.4	-1.7	-0.2	-0.6	3.5	-1.5	-1.3	-0.9	-0.6	0.6	-0.5
<b>Tyr</b>	0.9	1.5	-1.9	-0.5	-1.8	2.7	-1.8	1.7	0.7	0.9	0.2	-0.9
<b>Val</b>	8.8	-7.8	-1.2	0.2	2.3	5.8	-1.0	-9.5	-4.2	-5.1	0.1	2.0