SUPPLEMENTARY INFORMATION for

**Structure and Reorientational Dynamics of Angiotensin I and II: A
Microscopic Physical Insight**

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This Supplementary Information file contains additional results describing the molecular dynamics simulations of the angiotensin peptides.

Table S1. Average solvent accessible surface areas for the residues of angiotensins from 2 μ s MD simulations with OPLS-AA force field. Units: $\text{\AA}^2$.

Residue	ANGIn	ANGIp	ANGIIIn	ANGIIp
1	164 ± 17	150 ± 22	167 ± 13	161 ± 18
2	174 ± 30	174 ± 28	178 ± 28	178 ± 27
3	126 ± 18	128 ± 21	126 ± 17	123 ± 19
4	166 ± 27	168 ± 21	164 ± 22	166 ± 23
5	145 ± 19	130 ± 20	146 ± 16	141 ± 19
6	131 ± 20	117 ± 26	127 ± 24	128 ± 23
7	98 ± 17	107 ± 14	120 ± 10	119 ± 10
8	163 ± 27	179 ± 25	223 ± 24	226 ± 23
9	150 ± 23	153 ± 19		
10	195 ± 21	186 ± 23		

The data in Table S1 show that the main effect of statistical significance is the increase in accessible surface area of Phe8 upon peptide truncation.

Table S2. Conformational preferences of individual residues in the OPLS-AA trajectories of angiotensin peptides. Populations are calculated within circles of 60° radius around idealized structures in the Ramachandran map, as described in Methods. Data shown as free energy differences at 300 K, in kcal/mol, with the PPII conformation as reference. The typical statistical errors are about 0.1-0.3 kcal/mol for ΔG values below 0.5 kcal/mol, 0.3-0.4 kcal/mol for values of 0.5-1.0 kcal/mol, and 20-30% for values above 1.0 kcal/mol, respectively. “-” denotes cases where conformer was not detected.

Residue	AngI			AngIp			AngII			AngIIp		
	β	α_R	α_L	β	α_R	α_L	β	α_R	α_L	β	α_R	α_L
2	0.3	1.9	1.8	0.3	1.2	2.0	0.3	1.7	2.1	0.3	1.4	1.6
3	0.2	0.4	-	0.1	-0.6	-	0.1	0.6	-	0.1	0.5	-
4	-0.2	0.5	-	-0.2	-0.8	0.1	-0.2	0.6	-	-0.3	0.0	-
5	0.1	0.3	-	0.2	0.6	-	0.2	0.5	-	0.3	0.7	-
6	0.3	-	-	0.1	-	-	0.2	-	-	0.1	-	5.0
7	1.1	1.3	-	1.2	1.9	-	1.3	1.1	-	1.3	0.8	-
8	-0.1	0.5	4.4	0.0	0.8	0.0						
9	0.2	1.0	-	-0.3	2.4	0.8						
Average	0.2	0.9	3.0	0.2	0.6	1.3	0.3	1.0	3.2	0.2	0.8	2.6

This table shows that most residues are highly flexible, populating structures from three conformational basins. Several other effects that stand out: a) His6 tends to populate mostly the extended structures, PPII and β , with negligible contributions from α ; b) while the PPII structure predominates on average, Tyr4 exhibits a systematic preference for β ; c) only a few residues sample the α_L conformation – a small population is found for Arg2 in all four systems, Phe8 in ANGI_n and His6 in ANGII_p, while the largest populations are for Tyr4 and Phe8 in ANGI_p. Further structural analysis (not shown) indicates that a majority of peptide structures with left-handed content involve α_L conformations at one residue only. In the case of ANGI_p, which exhibits the largest average α_L population (6%, see Table 4) there is a small contribution (1 %) of structures with two residues in α_L simultaneously.

Figure S1: Distributions of measures of peptide size in the angiotensin MD trajectories. (A) C α 1...C α 8 distance (B) radius of gyration (C) Tyr4...Arg2 sidechain distance (D) Tyr4...His6 sidechain distance (E) Tyr4...Phe8 sidechain distance. Units: Å. Black-ANGIn, Red-ANGIp, Green-ANGIIIn, Blue-ANGIIp.

S1A

S1B

S1C

S1D

S1E

Figure S2: Autocorrelation functions of axis vectors describing peptide reorientations in the angiotensin MD simulations. (A) ANGIIn end-to-end distance (black,solid) and Tyr transition dipole (black,dotted), compared with ANGIIn end-to-end distance (grey,solid) and Tyr transition dipole (grey, dotted). (B) ANGIp end-to-end distance (black,solid) and Tyr transition dipole (black,dotted), compared with ANGIp end-to-end distance (grey,solid) and Tyr transition dipole (grey, dotted).

S2A

S2B

Figure S3. Ramachandran maps showing the distribution of backbone (ϕ, ψ) dihedrals in the 2 μ s MD simulations. Probability distribution for residues 2-9 of angiotensin I and residues 2-7 of angiotensin II converted to a potential of mean force at 300 K, in kcal/mol units.

S3A. AngI simulation

S3B. AngII simulation

S3C. AngIp simulations

S3D. AngIp simulation

Figure S4. Cluster population histories from our 2 μ s MD simulations of angiotensins in explicit solvent. Vertical axis shows the cluster numbers for clusters with 3 Å radius based on backbone atom RMSD.

S4A. AngI simulation

S4B. AngII simulation

S4C. AngIp simulation

S4D. AngIip simulation