Supporting Information for:

Molecular Dynamics of a Hydrated Collagen Peptide: Insights into Rotational Motion and Residence Times of Single Water Bridges in Collagen

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Here we present the results for all nine bridge sites and all four harmonic constraint values used. As the data presented is extensive, we have used a consistent colouring code to distinguish between constraint values:

Colour	k (kcal mol^{-1} Å^{-2})
Blue	0.1
Green	1
Orange	5
Red	10

DISTANCES

Distance between Collagen Atoms in Bridge Groups

		1	2	3	4	5	6	7	8	9
Carboxyl Oxygen to Amide Hydrogen Distance (Å)	Mean	4.23	4.11	4.19	4.18	4.17	4.28	4.09	4.09	4.07
	Standard Deviation	0.31	0.35	0.35	0.34	0.36	0.38	0.31	0.29	0.30
	Mean	4.12	3.89	4.16	3.99	4.08	4.06	4.00	4.02	4.11
	Standard Deviation	0.22	0.23	0.25	0.23	0.24	0.24	0.23	0.22	0.23
	Mean	4.07	3.88	4.25	4.01	4.13	4.08	4.04	4.06	4.14
	Standard Deviation	0.16	0.16	0.17	0.16	0.17	0.17	0.17	0.16	0.17
	Mean	4.05	3.88	4.27	4.04	4.15	4.09	4.05	4.07	4.15
	Standard Deviation	0.14	0.13	0.15	0.14	0.15	0.14	0.14	0.14	0.15

Table S1. *Mean distance and standard deviation between the carboxyl oxygen and the amide hydrogen of the nine different bridge sites. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*

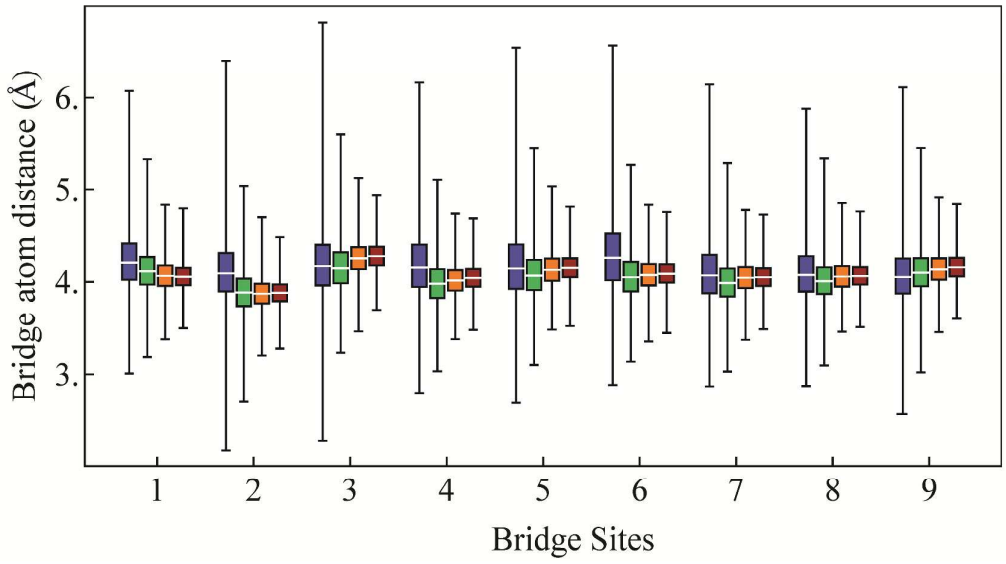

Figure S1. *Distributions of the distance between the carboxyl oxygen and the amide hydrogen of the nine different bridge sites for the 10 ns simulations. Boxes show the 25th to 75th percentiles, the white line is the median value. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*

Distance between Collagen Atoms and Water Molecules

		1	2	3	4	5	6	7	8	9
$d_{N-H\ldots O}$ (Å)	Mean	2.31 (2.10)	2.35 (2.07)	2.36 (2.09)	2.33 (2.05)	2.31 (2.06)	2.33 (2.05)	2.27 (2.05)	2.22 (2.05)	2.19 (2.04)
	Maxima	2.05 (2.05)	2.02 (2.02)	2.04 (2.04)	1.96 (2.00)	2.00 (1.98)	1.97 (2.03)	1.99 (2.00)	2.01 (2.01)	1.98 (1.98)
	Mean	2.24 (2.09)	2.31 (2.05)	2.36 (2.12)	2.22 (2.04)	2.22 (2.05)	2.23 (2.05)	2.14 (2.03)	2.08 (2.02)	2.17 (2.04)
	Maxima	2.12 (2.05)	1.99 (2.00)	2.10 (2.10)	1.95 (1.95)	1.99 (2.00)	1.96 (1.97)	1.98 (1.98)	1.98 (1.98)	1.97 (2.02)
	Mean	2.25 (2.09)	2.26 (2.05)	2.33 (2.14)	2.22 (2.05)	2.00 (2.06)	2.22 (2.07)	2.16 (2.04)	2.11 (2.04)	2.11 (2.05)
	Maxima	2.06 (2.06)	2.00 (1.94)	2.11 (2.11)	1.95 (2.00)	2.03 (2.03)	2.00 (2.00)	1.95 (2.01)	2.01 (2.01)	2.00 (2.01)
	Mean	2.24 (2.09)	2.24 (2.05)	2.34 (2.16)	2.30 (2.06)	2.19 (2.06)	2.23 (2.07)	2.16 (2.04)	2.10 (2.04)	2.35 (2.08)
	Maxima	2.03 (2.03)	1.96 (1.96)	2.15 (2.15)	1.97 (1.97)	1.97 (2.04)	1.99 (2.02)	1.96 (1.98)	1.95 (1.98)	2.03 (2.03)

Table S2. *Mean distance and maxima value of the distribution of distances between the amide hydrogen and the oxygen atom in the closest water molecule to nine different bridge sites. Corresponding values for when a strict bridge is formed are shown in brackets. The closest water molecule to a bridge site is determined by Equation (2). Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*

		1	2	3	4	5	6	7	8	9
$d_{C=O\ldots H}$ (Å)	Mean	2.11 (1.91)	2.04 (1.89)	2.05 (1.91)	2.38 (1.94)	2.37 (1.94)	2.52 (1.95)	2.15 (1.91)	2.05 (1.91)	2.12 (1.91)
	Maxima	1.82 (1.82)	1.82 (1.83)	1.83 (1.83)	1.85 (1.83)	1.86 (1.86)	1.82 (1.86)	1.84 (1.84)	1.79 (1.83)	1.82 (1.82)
	Mean	2.02 (1.91)	2.00 (1.90)	2.07 (1.92)	2.22 (1.95)	2.20 (1.94)	2.29 (1.94)	2.11 (1.92)	2.12 (1.93)	2.17 (1.95)
	Maxima	1.83 (1.83)	1.80 (1.84)	1.85 (1.85)	1.86 (1.89)	1.85 (1.85)	1.81 (1.85)	1.81 (1.85)	1.83 (1.83)	1.84 (1.86)
	Mean	2.02 (1.91)	1.99 (1.90)	2.11 (1.98)	2.34 (2.00)	2.22 (1.96)	2.30 (1.95)	2.17 (1.94)	2.13 (1.95)	2.26 (1.99)
	Maxima	1.85 (1.85)	1.83 (1.83)	1.92 (1.92)	1.90 (1.90)	1.87 (1.87)	1.87 (1.87)	1.84 (1.89)	1.84 (1.84)	1.89 (1.92)
	Mean	2.00 (1.91)	1.97 (1.90)	2.14 (2.00)	2.41 (2.00)	2.26 (1.97)	2.31 (1.96)	2.21 (1.95)	2.12 (1.95)	2.19 (1.98)
	Maxima	1.81 (1.87)	1.80 (1.80)	1.88 (1.95)	1.86 (1.93)	1.85 (1.85)	1.84 (1.90)	1.84 (1.88)	1.84 (1.84)	1.86 (1.89)

Table S3. *Mean distance and maxima value of the distribution of distances between the carboxyl oxygen and the hydrogen atom (in the closest water molecule) closest to the carboxyl oxygen for the nine different bridge sites. Corresponding values for when a strict bridge is formed are shown in brackets. The closest water molecule to a bridge site is determined by Equation (2). Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*

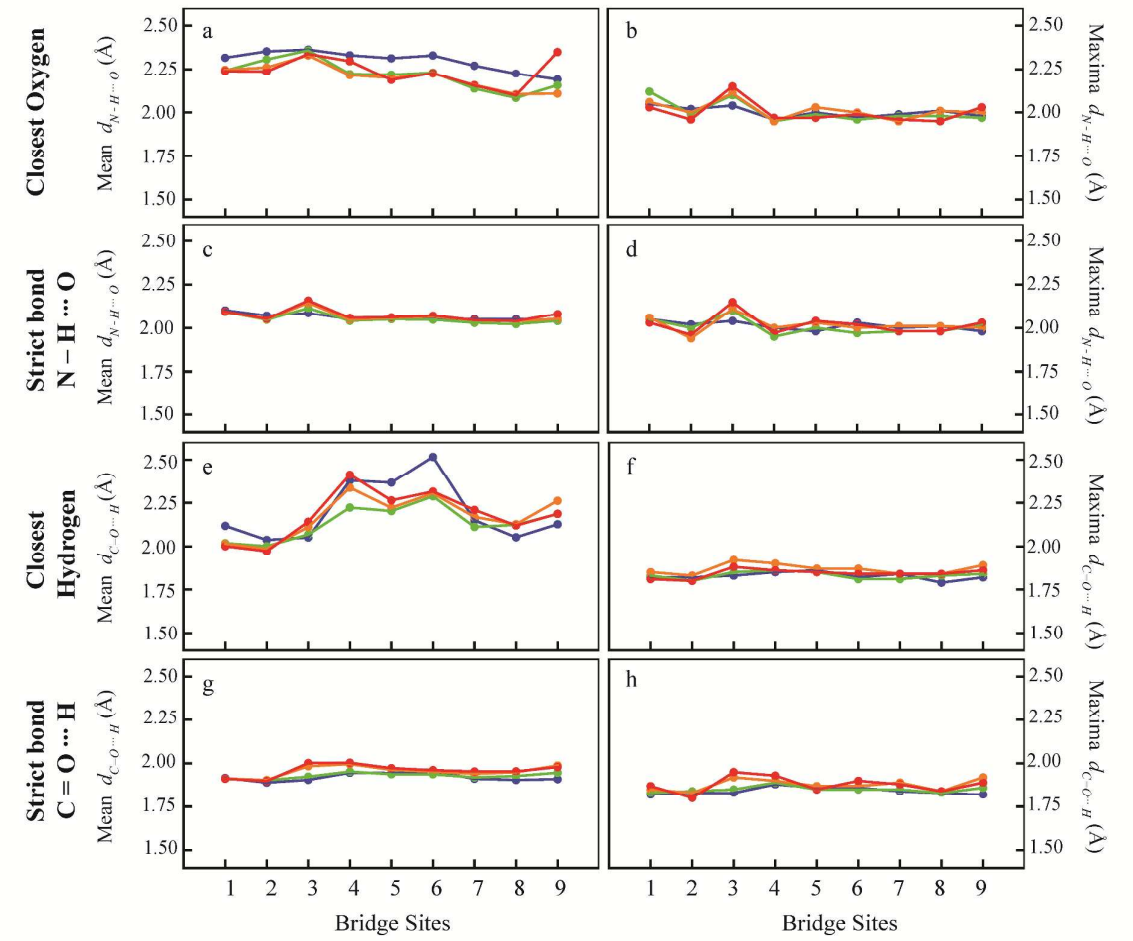

Figure S2. *Mean (left column) and Mode (right column) of the distributions of the distances between the closest water molecule to the nine bridge sites and the collagen bridge atoms. Shown are the distance between a) and b) the oxygen atom in the closest water and the amide hydrogen; c) and d) the oxygen atom in the closest water and the amide hydrogen when a strict hydrogen bond is formed; e) and f) the closest hydrogen atom in the closest water and the carboxyl oxygen; g) and h) the closest hydrogen atom in the closest water and the carboxyl oxygen when a strict hydrogen bond is formed.*

RESIDENCE TIMES AND OCCUPANCIES

		1	2	3	4	5	6	7	8	9
Closest Water Residence Time (ps)	Mean	8.71	7.23	9.54	1.91	2.01	1.32	5.09	17.79	9.93
	Weighted Median	69.1	89.0	100.4	19.2	14.4	7.6	38.3	110.8	87.9
	Mean*	18.80	9.39	6.79	3.68	4.65	2.96	9.30	23.81	17.92
	Weighted Median *	132.2	78.5	101.2	36.9	37.4	21.3	63.6	144.7	140
	Mean	14.39	14.00	8.25	3.67	6.19	4.18	8.59	26.88	27.25
	Weighted Median	174.2	111.1	87.6	34.0	17.3	26.8	63.2	145.2	125.0
	Mean	17.15	16.89	8.36	2.42	5.77	4.21	7.08	46.08	15.01
	Weighted Median	159.7	127.7	72.0	25.4	42.2	28.8	44.3	210.2	95.2

Table S4. *Mean and time-weighted median residence times of the closest water to each bridge site (determined from Equation (2)).Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*Shown in Table 1 in manuscript.*

		1	2	3	4	5	6	7	8	9
Closest Hydrogen Residence Time (ps)	Mean	4.27	4.40	4.89	1.25	1.23	0.82	2.76	5.49	4.14
	Weighted Median	28.1	34.7	36.0	10.6	6.3	3.4	16.5	22.9	20.7
	Mean*	8.54	5.32	4.34	2.34	2.67	1.76	4.11	5.63	4.43
	Weighted Median *	45.3	36.1	46.0	18.4	15.0	9.8	20.2	22.0	17.9
	Mean	7.11	6.93	4.44	2.27	3.01	2.29	3.41	5.38	3.97
	Weighted Median	54.8	39.7	35.3	16.4	15.6	12.4	17.3	19.7	14.7
	Mean	7.52	8.47	4.29	1.66	2.63	2.27	3.28	6.23	4.03
	Weighted Median	48.5	52.3	30.8	13.1	13.7	11.5	16.3	20.4	15.0

Table S5. *Mean and time-weighted median residence times of the closest hydrogen atom, in the closest water, to the carboxyl oxygen at each bridge site. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*Shown in Table 1 in manuscript.*

		1	2	3	4	5	6	7	8	9
Strict N – H ··· O	Occupancy	0.74	0.72	0.70	0.76	0.76	0.76	0.77	0.83	0.86
	Mean Time (ps)	0.73	0.86	0.73	0.95	0.93	0.92	1.08	1.28	1.52
	Time-Weighted Median (ps)	1.4	1.9	1.4	1.9	1.7	1.8	2.4	2.7	3.1
	Occupancy*	0.80	0.75	0.69	0.82	0.83	0.82	0.88	0.92	0.88
	Mean Time (ps)*	0.86	1.05	0.56	1.21	1.19	1.13	1.64	2.18	1.72
	Time-Weighted Median (ps)*	1.6	2.2	1.0	2.4	2.4	2.2	3.2	4.5	3.7
	Occupancy	0.80	0.77	0.70	0.82	0.84	0.82	0.87	0.91	0.91
	Mean Time (ps)	0.88	1.00	0.50	1.21	1.23	1.18	1.58	1.99	1.86
	Time-Weighted Median (ps)	1.6	2.1	0.8	2.6	2.4	2.2	3.2	4.2	3.7
	Occupancy	0.80	0.79	0.69	0.77	0.85	0.82	0.88	0.92	0.79
	Mean Time (ps)	0.88	1.05	0.47	1.02	1.26	1.14	1.60	2.13	1.23
	Time-Weighted Median (ps)	1.6	2.3	0.7	2.2	2.5	2.3	3.2	4.3	2.9

Table S6. *Mean and time-weighted median residence times of the water oxygen, in the closest water molecule, making a strict bond ($d_{N-H\cdots O} < 2.4$) with the amide hydrogen at each of the bridge sites. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*Shown in Table 1 in manuscript.*

		1	2	3	4	5	6	7	8	9
Strict C = O ··· H	Occupancy	0.83	0.88	0.88	0.68	0.66	0.56	0.8	0.86	0.81
	Mean Time (ps)	2.07	2.67	2.5	1.08	0.93	0.71	1.75	2.15	1.72
	Time-Weighted Median (ps)	5.2	7.1	6.2	3.0	2.5	2.1	4.7	5.4	4.8
	Occupancy*	0.89	0.91	0.87	0.76	0.77	0.72	0.82	0.81	0.77
	Mean Time (ps)*	2.56	2.36	2.40	1.29	1.38	1.18	1.70	1.55	1.24
	Time-Weighted Median (ps)*	6.1	5.3	6.2	2.9	3.3	3.0	4.3	3.8	3.1
	Occupancy	0.90	0.91	0.86	0.68	0.76	0.70	0.78	0.81	0.71
	Mean Time (ps)	2.73	2.50	1.72	0.90	1.22	1.20	1.43	1.35	0.89
	Time-Weighted Median (ps)	6.6	5.7	3.7	1.8	2.7	3.0	3.5	3.1	2.0
	Occupancy	0.91	0.92	0.84	0.63	0.72	0.69	0.76	0.82	0.77
	Mean Time (ps)	2.94	2.63	1.5	0.82	1.1	1.14	1.3	1.37	1.14
	Time-Weighted Median (ps)	7.3	6.5	3.1	1.8	2.5	2.8	3.2	3.1	2.8

Table S7. *Mean and time-weighted median residence times of the closest water hydrogen, in the closest water molecule, making a strict bond ($d_{C=O\cdots H} < 2.4$) with the carboxyl oxygen at each of the bridge sites. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*Shown in Table 1 in manuscript.*

		1	2	3	4	5	6	7	8	9
Strict Bridge	Occupancy	0.62	0.64	0.61	0.48	0.46	0.37	0.60	0.71	0.69
	Mean Time (ps)	0.58	0.72	0.60	0.65	0.57	0.55	0.73	0.83	0.86
	Time-Weighted Median (ps)	1.0	1.4	1.1	1.1	1.0	1.0	1.4	1.5	1.6
	Occupancy*	0.72	0.69	0.60	0.61	0.63	0.57	0.72	0.74	0.67
	Mean Time (ps)*	0.68	0.76	0.48	0.72	0.72	0.70	0.92	0.94	0.72
	Time-Weighted Median (ps)*	1.2	1.4	0.8	1.2	1.2	1.2	1.6	1.8	1.3
	Occupancy	0.73	0.71	0.59	0.54	0.63	0.56	0.68	0.74	0.64
	Mean Time (ps)	0.71	0.74	0.39	0.54	0.66	0.64	0.81	0.81	0.59
	Time-Weighted Median (ps)	1.2	1.3	0.6	0.9	1.1	1.1	1.5	1.5	1.0
	Occupancy	0.74	0.74	0.57	0.45	0.60	0.55	0.66	0.75	0.58
	Mean Time (ps)	0.71	0.77	0.35	0.48	0.63	0.60	0.78	0.82	0.52
	Time-Weighted Median (ps)	1.2	1.4	0.5	0.8	1.1	1.0	1.4	1.5	0.9

Table S8. *Mean and time-weighted median residence times of water molecules making a strict water bridge ($d_{N-H\cdots O} < 2.4$ and $d_{C=O\cdots H} < 2.4$) at each of the bridge sites. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*Shown in Table 1 in manuscript.*

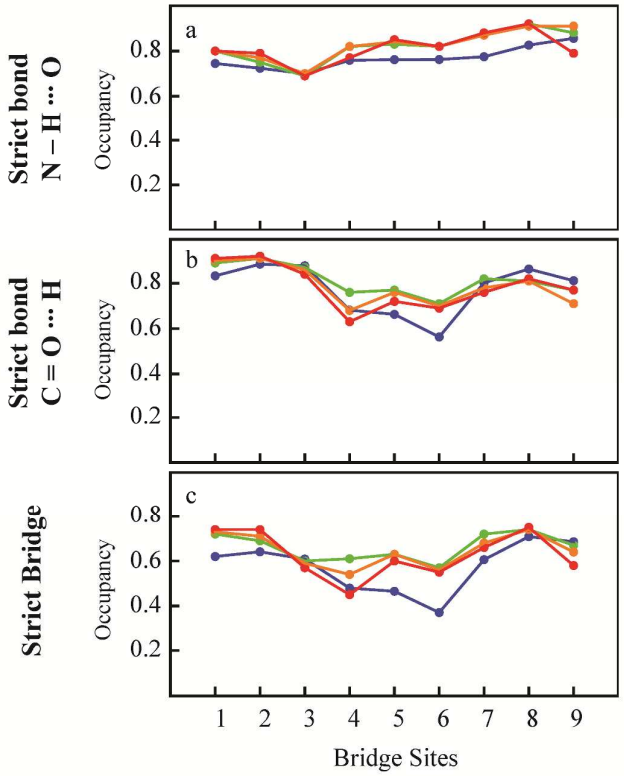

Figure S3. *Occupancies of the three bond states with strict hydrogen bonds; a) the bond between water oxygen in the closest water and the amide hydrogen; b) the bond between a water hydrogen and the carboxyl oxygen; c) the strict bridge state where with both hydrogen bonds. The occupancies in a) and b) include instances were a strict bridge is formed.*

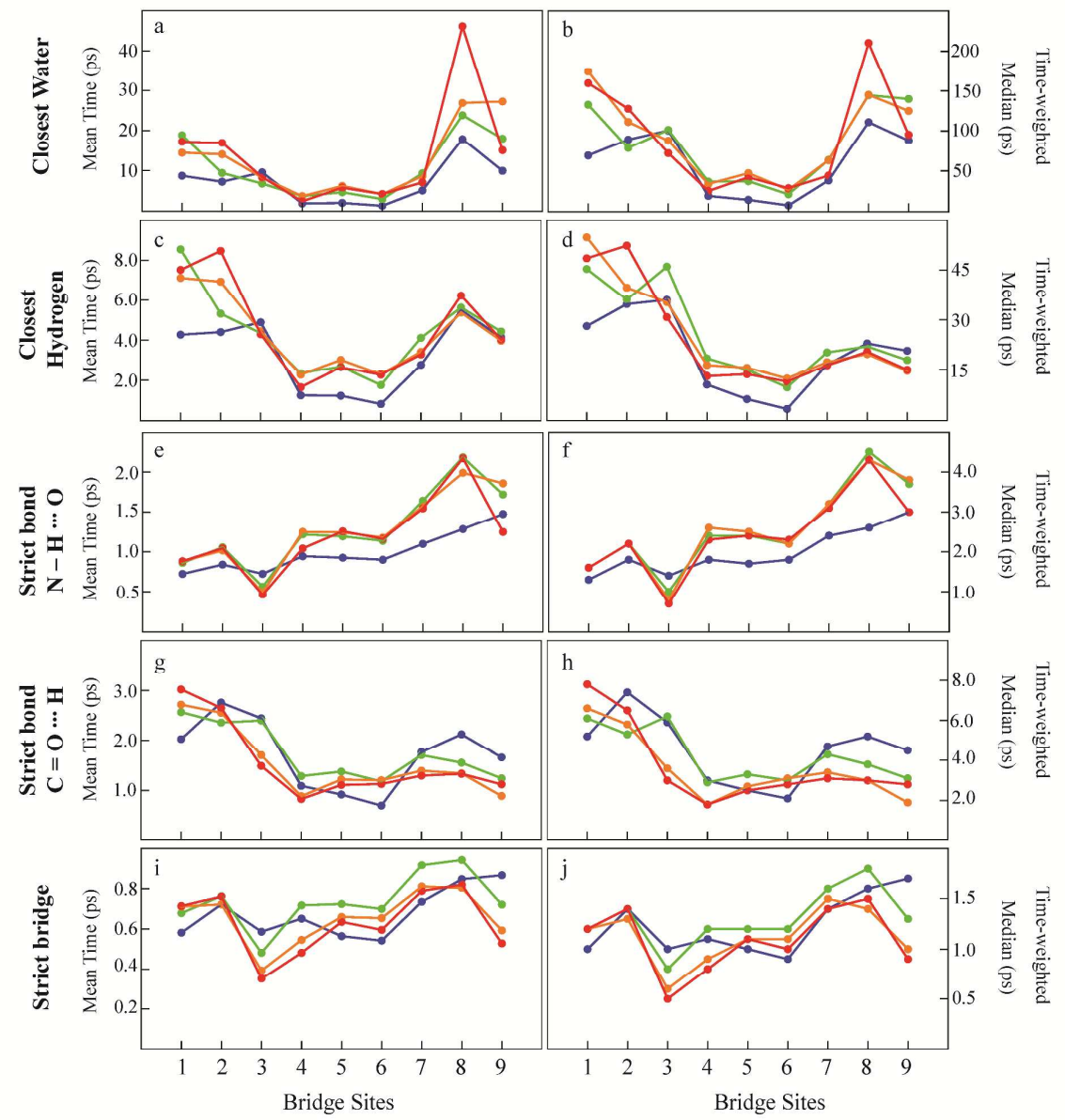

Figure S4. *Residence time of all five bond state; a) and b) the closest water molecule to the bridge site determined from equation 2; c) and d) the hydrogen atom, in the closest water molecule, closest to the carboxyl oxygen; e) and f) a strict bond ($d_{N-H...O} < 2.4$) between the water oxygen in the closest water and the amide hydrogen; g) and h) a strict bond ($d_{C=O...H} < 2.4$) between a water hydrogen in the closest water and the carboxyl oxygen; a strict bridge ($d_{N-H...O} < 2.4$ and $d_{C=O...H} < 2.4$). Number-weighted mean times are shown in the left column; time-weighted median times are shown in the right column. Colours correspond to the different backbone constraints.*

WATER BRIDGE ENERGIES

The ten water molecules that spent the longest time as the closest water molecule to each bridge site were identified. The energies of the ten water molecules while they were at the bridge site were calculated. The average, mean energy of 50 bulk water molecules from a 900 ps bulk water simulation was (-9.63 ± 0.04) kcal mol^{-1}; the average standard deviation was (-1.74 ± 0.02) kcal mol^{-1}.

	1	2	3	4	5	6	7	8	9
Mean Energy (kcal mol^{-1})	-10.05	-10.15	-10.21	-11.28	-10.52	-10.90	-10.36	-9.96	-9.66
Standard Deviation (kcal mol^{-1})	1.61	1.57	1.62	1.54	1.69	1.70	1.69	1.50	1.46
Mean Energy (kcal mol^{-1})	-10.21	-10.38	-10.82	-11.29	-10.76	-10.90	-10.17	-9.76	-9.43
Standard Deviation (kcal mol^{-1})	1.66	1.56	1.61	1.51	1.70	1.66	1.61	1.43	1.41
Mean Energy (kcal mol^{-1})	-10.21	-10.28	-10.76	-11.03	-10.59	-10.64	-10.09	-9.67	-9.32
Standard Deviation (kcal mol^{-1})	1.69	1.60	1.49	1.56	1.71	1.75	1.69	1.39	1.39
Mean Energy (kcal mol^{-1})	-10.20	-10.29	-10.80	-11.09	-10.57	-10.62	-10.24	-9.59	-9.24
Standard Deviation (kcal mol^{-1})	1.68	1.56	1.50	1.48	1.70	1.76	1.67	1.38	1.46

Table S9. *The mean energy and standard deviations of water molecules at the bridge sties calculated across the ten water molecules which spent the longest times as the closest water molecule to a particular bridge site. Colours correspond to the different harmonic constraints used on the backbone collagen molecule.*

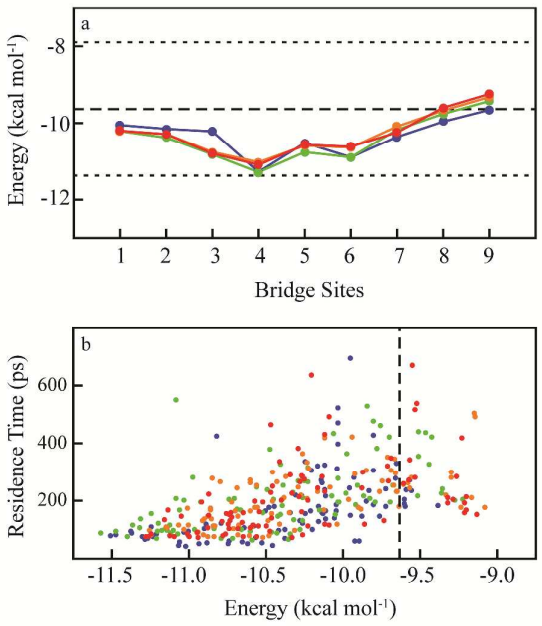

Figure S5. *a) The mean energy across all ten water molecules for each bridge site. The dashed line indicates the mean bulk water energy value; the dotted lines indicate the first standard deviation of the bulk water energy distribution. b) Relationship between the residence time of each of the ten water molecules for each bridge site and the mean energy of the water molecule during its time at the bridge site. (Colours correspond to the different backbone constraints).*

MOBILE-PROTON ROTATIONAL CORRELATION

The correlation functions of $\sin^2 \phi$ are shown below (right column) for the nine bridge sites, with the distribution of rotational angles, ϕ, (left column) of the mobile O-H vector around the mean bridge O-H vector axis. The histograms below are shown as lines for clarity. Error bars in the correlation curves are standard errors, not standard deviations. Only data for the closest water molecule is shown, data for the case when a strict bridge is formed is not shown. The bridges are broken up into four groups according to similar rotational motion; bridge1; bridges 2, 3 and 4; bridges 5, 6 and 7; bridges 8 and 9.

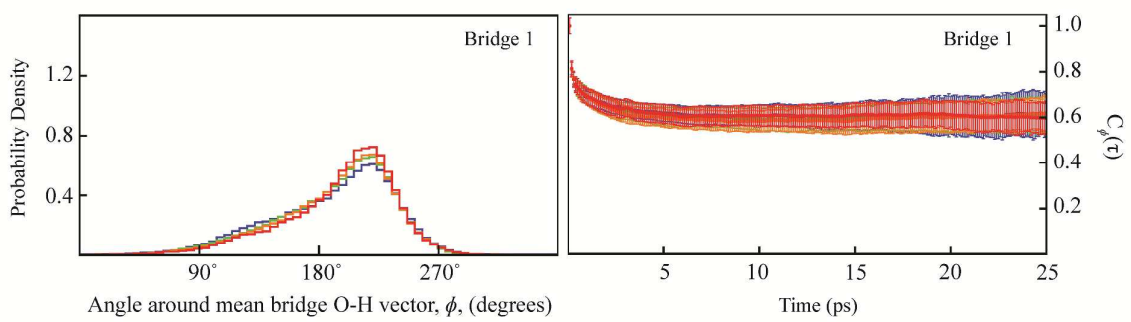

Figure S6. *Rotation of the mobile O-H vector around the mean bridge O-H vector for water molecules at bridge site 1. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*

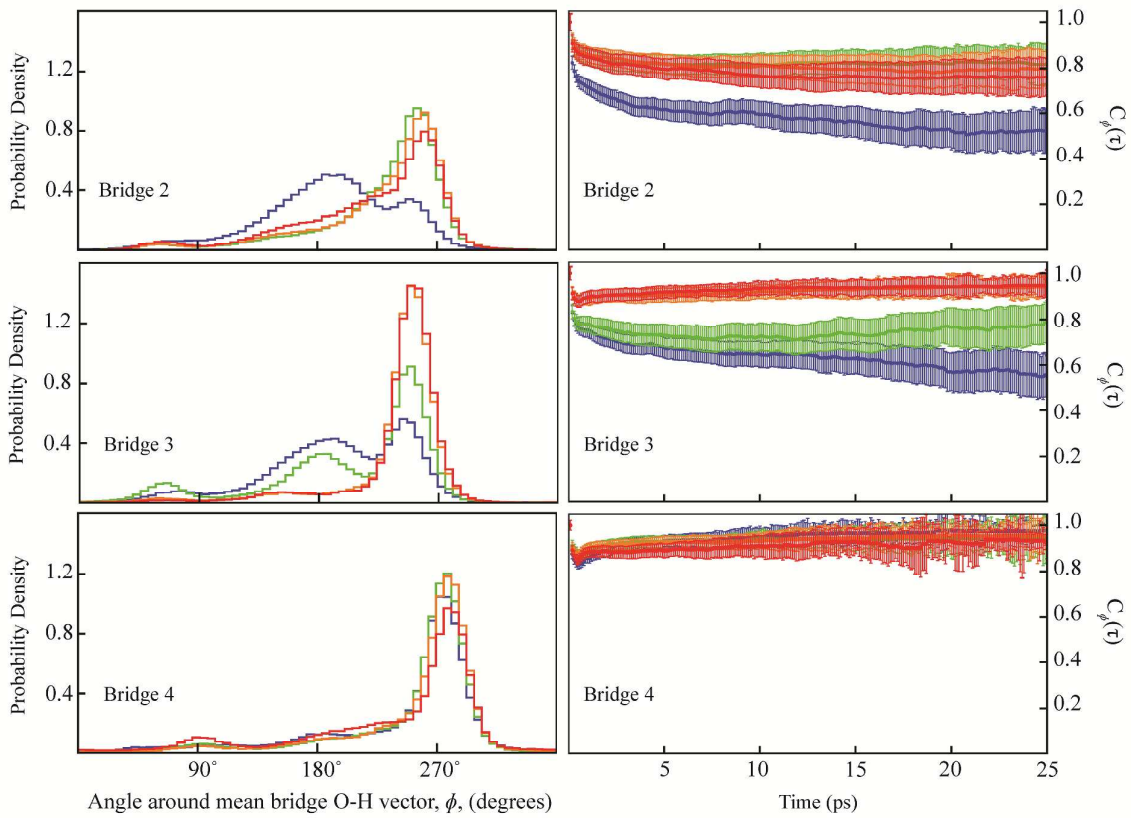

Figure S7. *Rotation of the mobile O-H vector around the mean bridge O-H vector for water molecules at bridge site 2, 3 and 4. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*

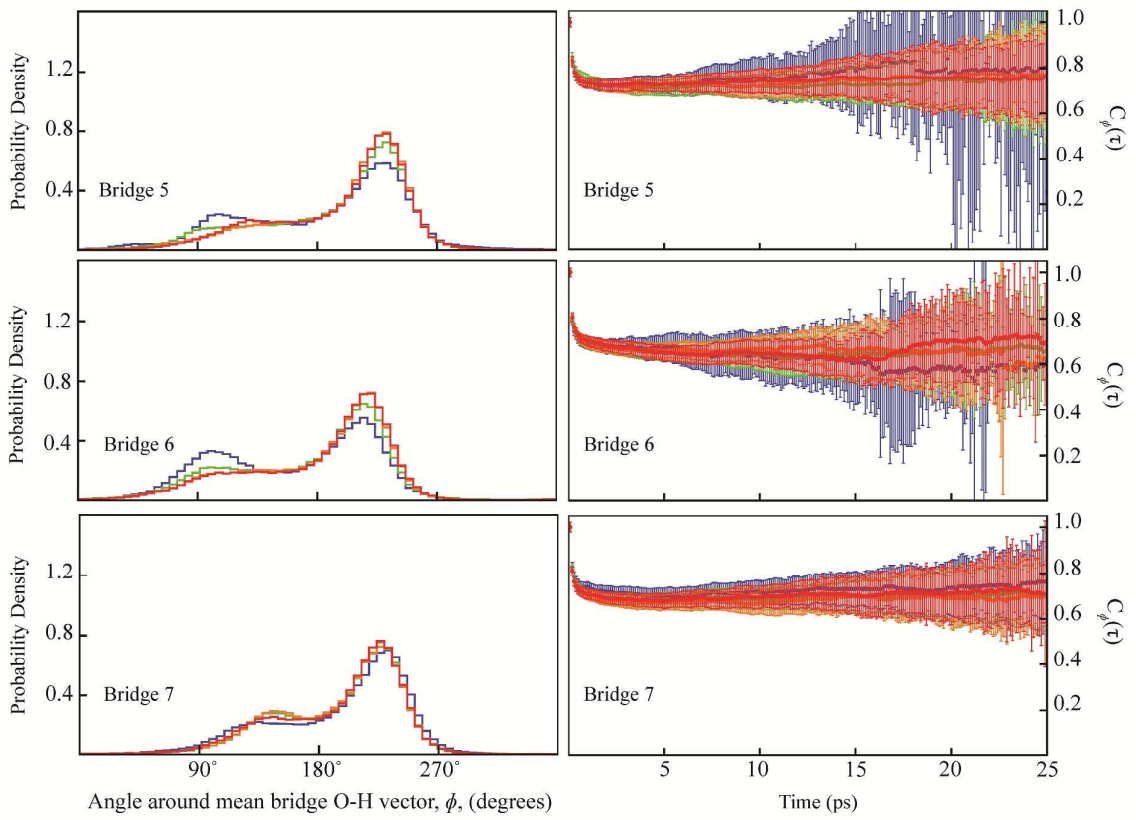

Figure S8. *Rotation of the mobile O-H vector around the mean bridge O-H vector for water molecules at bridge site 2, 3 and 4. Error bars are large in these groups as a result of shorter closest hydrogen times (Table S5). Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*

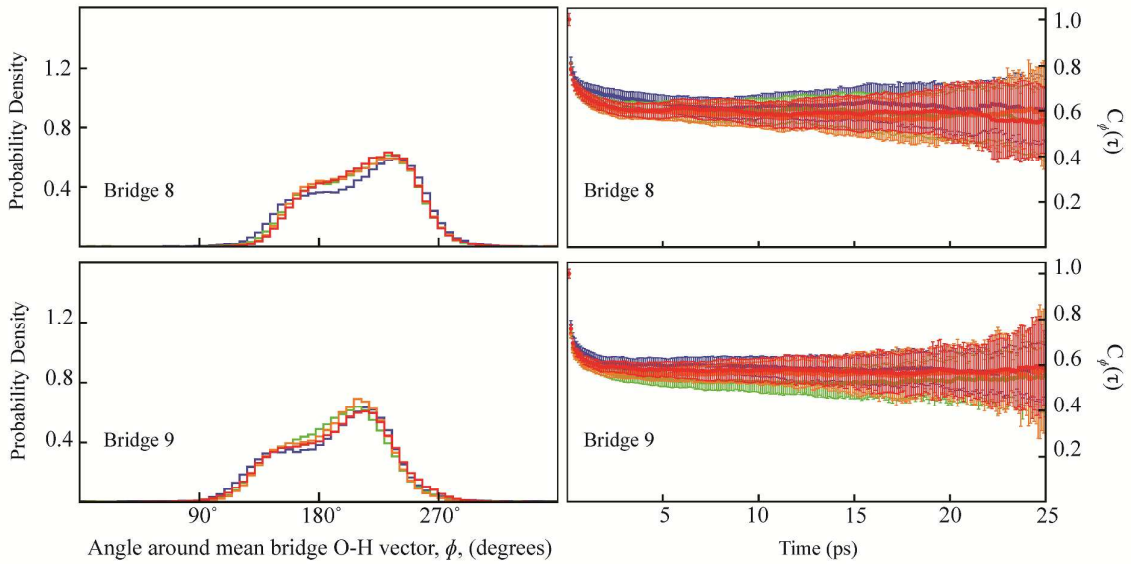

Figure S9. *Rotation of the mobile O-H vector around the mean bridge O-H vector for water molecules at bridge site 2, 3 and 4. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*

INTRA-PROTON VECTOR ROTATIONS

	1	2	3	4	5	6	7	8	9	<H-H>
Closest Water	69.3	68.2	56.5	32.2	62.0	63.02	60.0	64.6	65.2	17.5
Strict Bridge	68.8	69.1	56.4	35.4	60.8	60.8	59.6	64.4	64.5	14.4
Closest Water*	70.4	46.0	46.9	33.9	61.6	63.3	62.1	66.1	66.4	15.9
Strict Bridge*	70.7	48.2	49.8	34.3	61.4	61.8	61.1	64.4	65.7	13.2
Closest Water	71.0	45.9	33.9	33.5	59.9	60.6	62.5	66.7	65.0	18.3
Strict Bridge	71.3	47.9	34.3	31.9	59.5	59.4	61.0	65.1	64.4	14.7
Closest Water	70.5	50.9	33.8	37.5	59.2	60.2	62.1	66.0	66.0	19.9
Strict Bridge	70.6	52.1	33.7	36.4	58.6	58.3	60.4	61.6	66.3	16.2

Table S10. *Angle between the z-axis (collagen axis) and the sum the intra-molecular H-H vectors throughout the 10 ns simulation. The angle between the z-axis and the total time-average H-H vector, <H-H> across all bridge sites is also shown. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*Shown in Table 1 in manuscript.*

This distribution of angles between the inter-proton vector of the closest water molecule and the z-axis for all nine groups are shown below. The bridges are separated into the same four groups according to rotational motion as above. The left column shows distributions when a strict bridge is formed, the right column includes all data points from the closest water molecules to the bridge site. The histograms below are shown as lines for clarity.

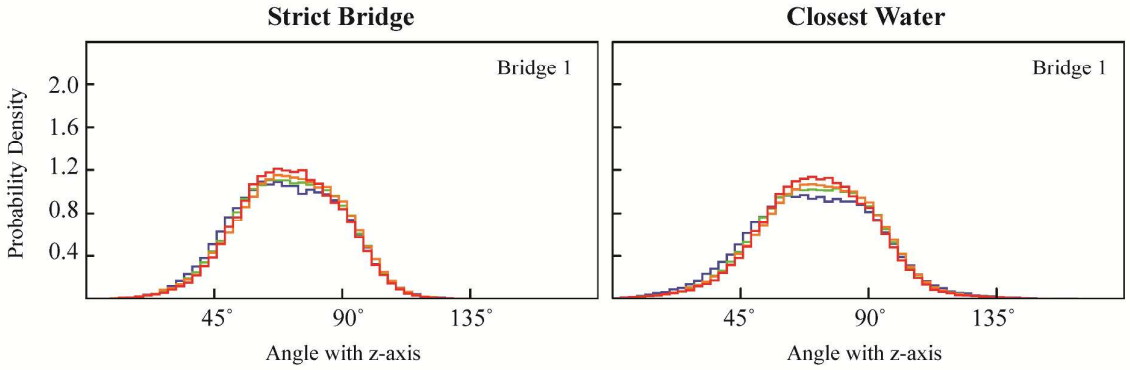

Figure S10. *Angle between z-axis and the H-H vector of the closest water molecule at Bridge 1. Colours correspond to the different harmonic constraints used on the backbone collagen molecules.*

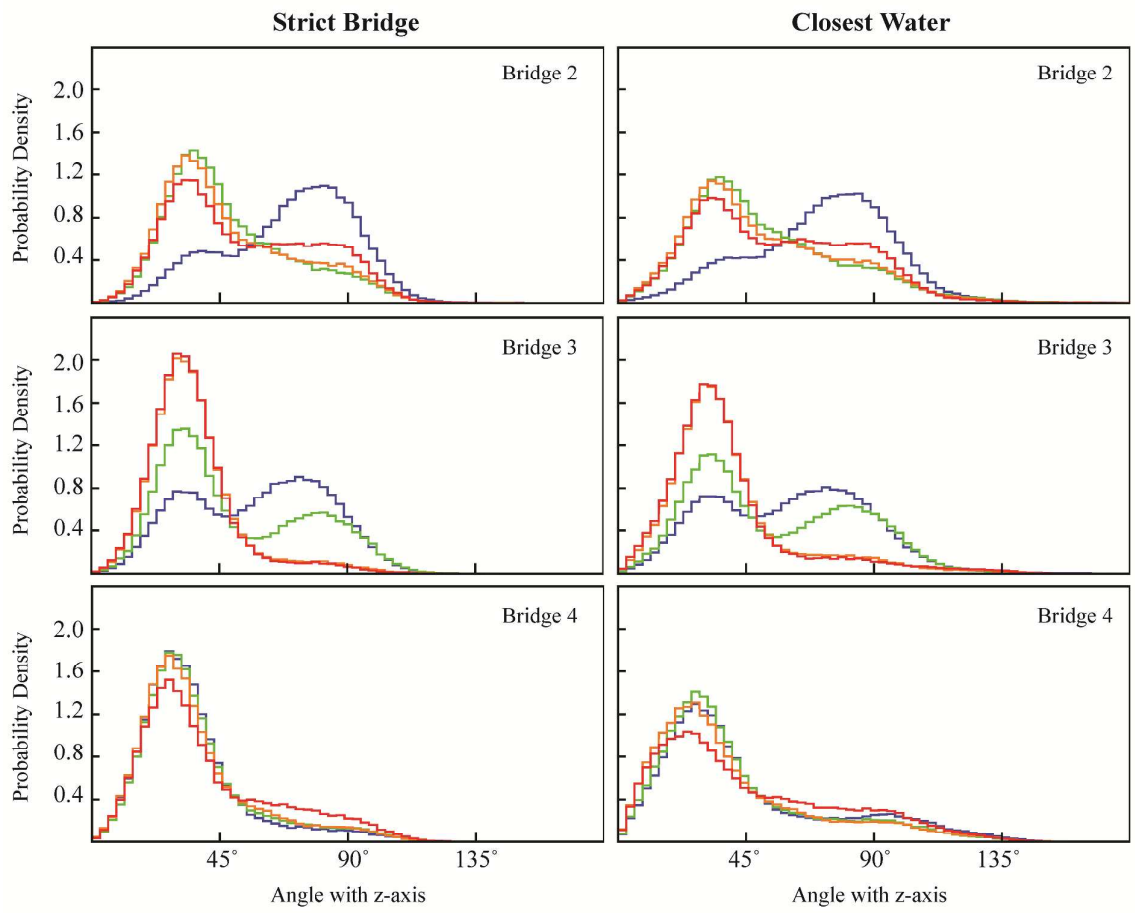

Figure S11. *Angle between z-axis and the H-H vector of the closest water molecule at Bridge 2, 3, 4. In addition to the bridge bonds, these water molecules may make a third bond with the THR OH group (see manuscript Figure 9). Colours correspond to the different harmonic constraints used on the backbone collagen molecules*

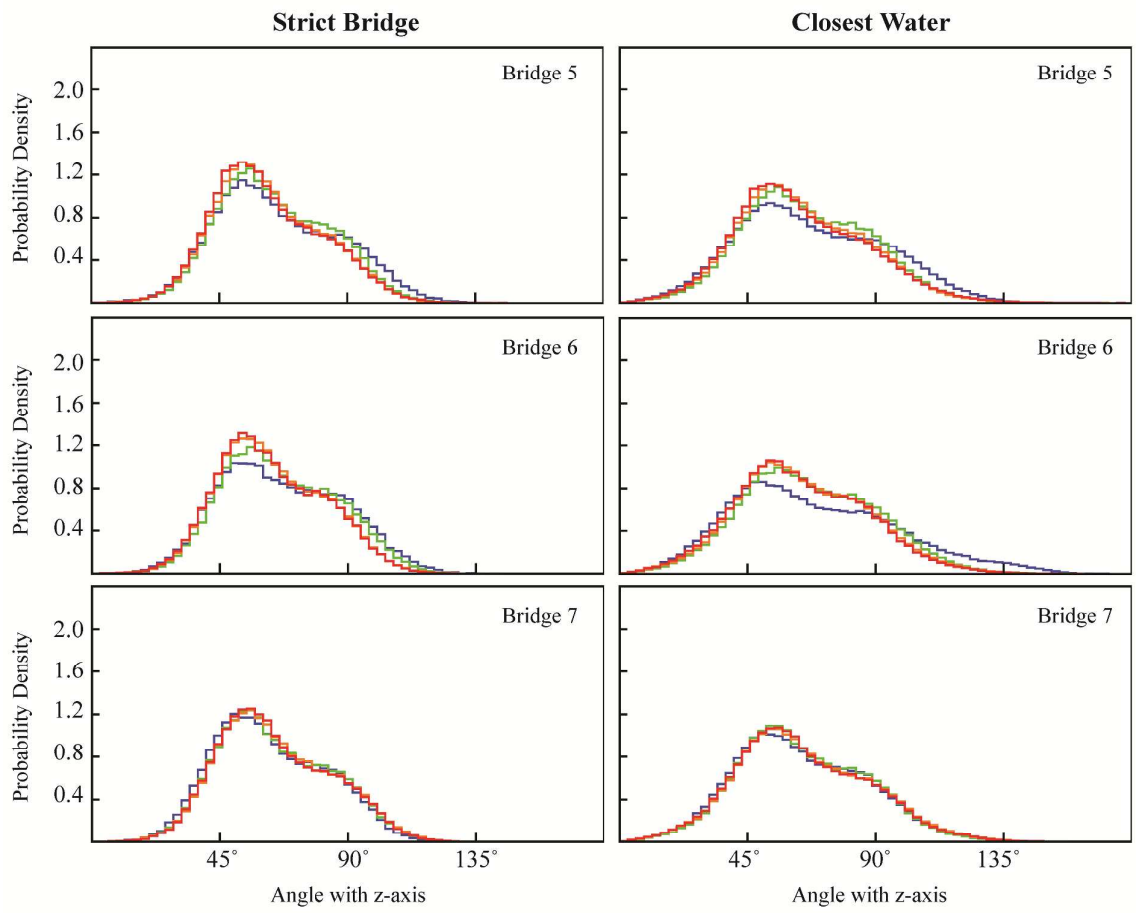

Figure S12. *Angle between z-axis and the H-H vector of the closest water molecule at Bridge 5,6, 7. Colours correspond to the different harmonic constraints used on the backbone collagen molecules*

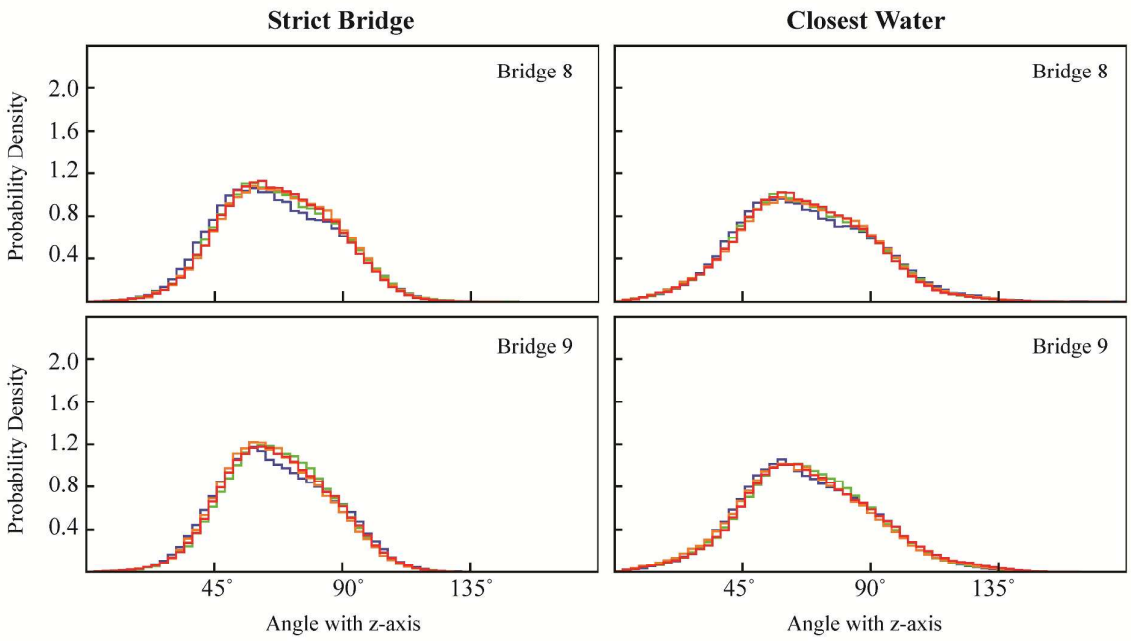

Figure S13. *Angle between z-axis and the H-H vector of the closest water molecule at Bridge 5,6, 7. Colours correspond to the different harmonic constraints used on the backbone collagen molecules*