Supplementary Information

Title: Modelling the interaction of a Hyp-Pro-Gly tri-peptide with hydroxyapatite in an aqueous environment

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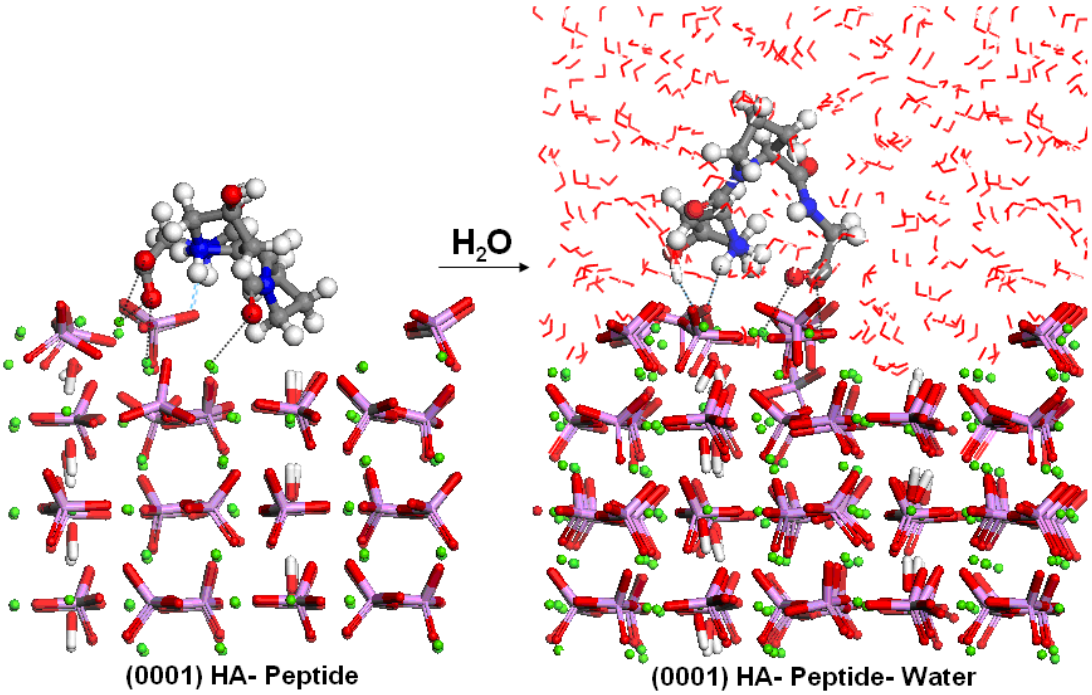

Surface Models

Having optimized the HA bulk structure, we have used the METADISE code[1] to create the surfaces, which were subsequently optimised using the molecular dynamics simulations in vacuum. In this study, we have concentrated on two of the most significant surfaces of the apatite bone mineral, namely the (0001) and $(01\bar{1}0)$ surfaces. These two surfaces are important in the morphology of the apatite mineral platelets and there is experimental evidence that these faces act as the binding site for many ionic species, including small molecules, polymers and anionically-modified cell surfaces[2, 3].

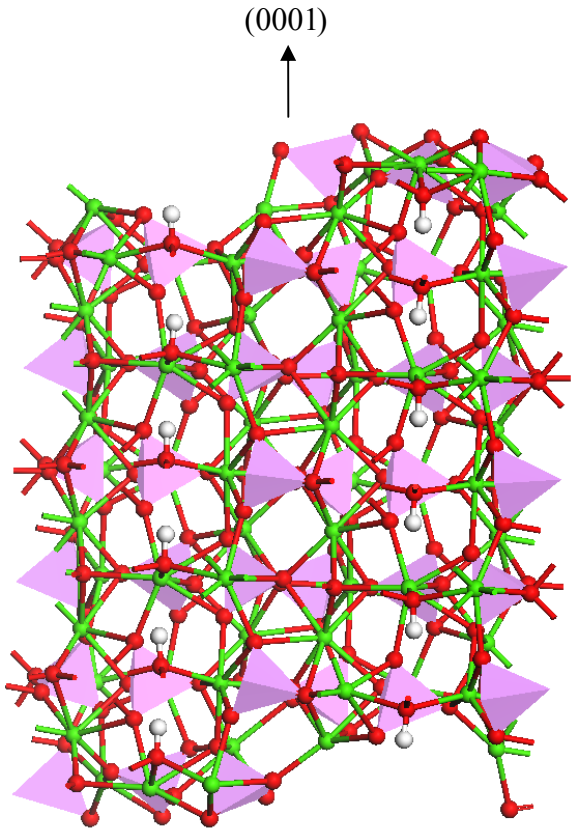

Figure S1. Relaxed surfaces of hydroxyapatite: (a) PO_4-Ca-PO_4-PO_4-Ca-Ca termination of the (0001) surface and (b) Ca-Ca in the bottom and (OH-OH-Ca-Ca) in the top of the $(01\bar{1}0)$ surface (Ca = green, O = red, P = purple, H = white).

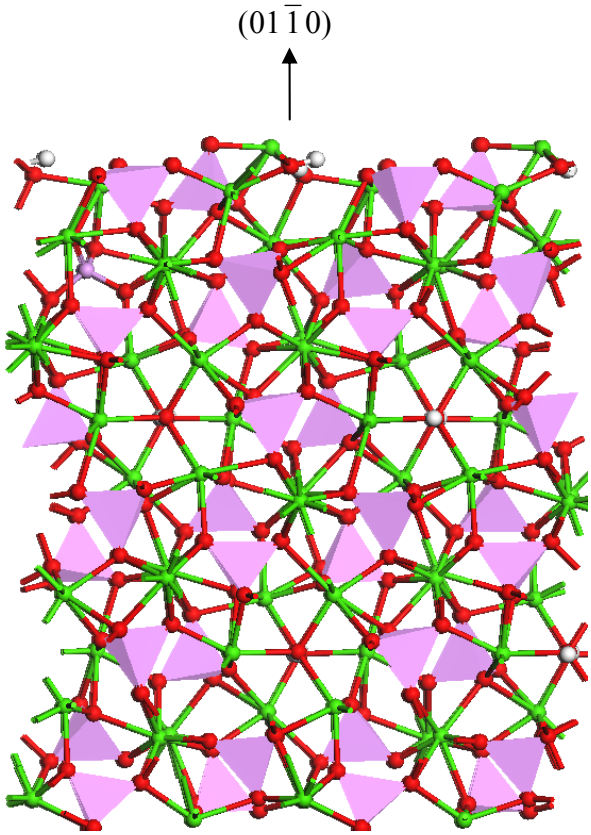

Figure S2. Calculated lowest energy structures of (a) glycine, (b) proline, (c) hydroxyproline, showing intramolecular hydrogen-bonding (C = grey, O = red, N = blue, H = white).

Definition of Atom Types

The peptide chain was constructed by linking the amino acids residues glycine-proline-hydroxyproline, which are a important residues of collagen type I. Figure S1 schematically showed the definition of atoms that were used in MD simulation.

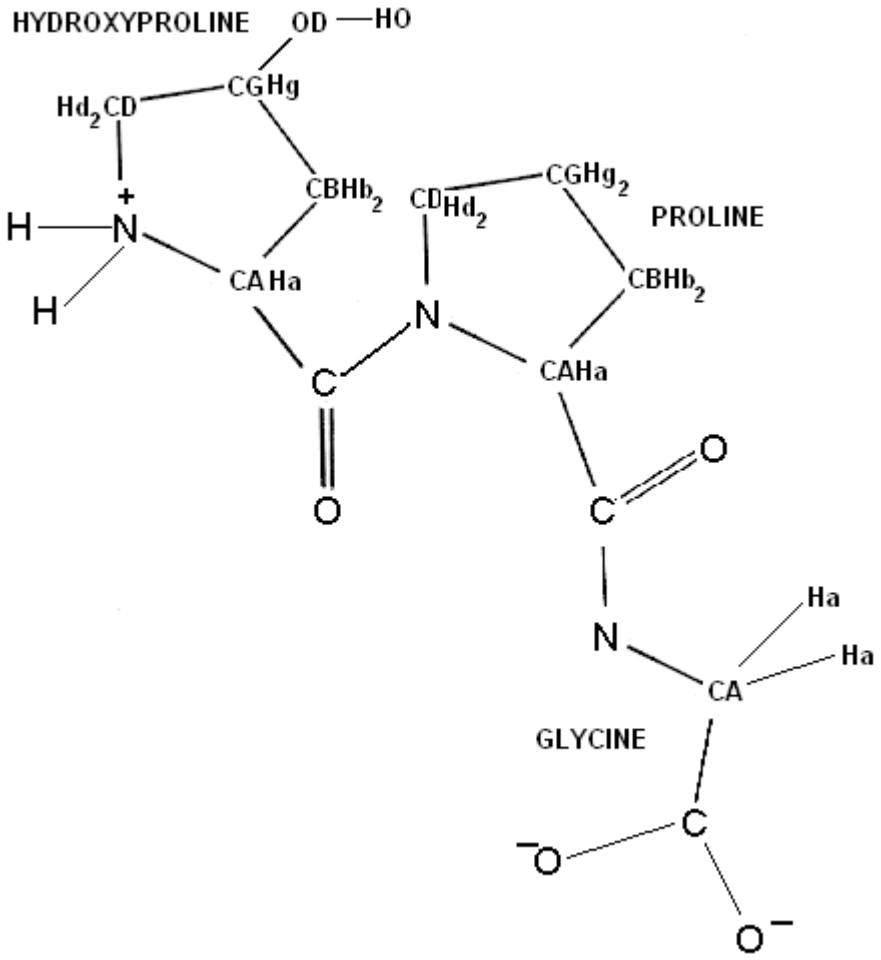

Figure S3 Schematic drawing of ($^{+}H_2N$-Hydroxyproline-Proline- Glycine-COO^{-}) peptide structure.

Table S1 Atom Charges

Ion	Charges (e)		Core-shell interaction eV Å^2	Comments
	Core	Shell		
Hydroxyapatite				de Leeuw et al.
Ca	+2.000			
P	+1.180			
Phosphate oxygen (O2)	+0.587	-1.632	507.4000	
Hydroxy oxygen (O1)	+0.900	-2.300	74.92038	
Hydroxy hydrogen (H1)	+0.400			
Water				TIP3P

Oxygen (OW)	-0.8340
Hydrogen (HW)	+0.4170

Hydroxyproline		AMBER
N	-0.2548	
CA	+0.0047	
C	+0.5896	
O	-0.5748	
CB	-0.0032	
CG	+0.0908	
CD	-0.0081	
OD	-0.5930	
Ha	+0.1135	
Hb	+0.1135	
Hg	+0.1135	
Hd	+0.1135	
HO	+0.4588	
H	+0.3045	
Proline		AMBER
N	-0.2548	
CA	-0.0266	
C	+0.5896	
O	-0.5748	
CB	-0.0070	
CG	+0.0189	
CD	+0.0192	
Ha	+0.0641	
Hb	+0.0253	
Hg	+0.0213	
Hd	+0.0391	
Glycine		AMBER
N	-0.3821	
CA	-0.2493	
C	+0.7231	
O	-0.7855	
Ha	+0.1056	
H	+0.2681	

The HA short-range interactions were described by an effective Buckingham potential (buck):

$$\Phi_{ij}\left(r_{ij}\right) = A_{ij}e^{-\frac{r_{ij}}{\rho_{ij}}} - \frac{C_{ij}}{r_{ij}^{6}} \quad (1)$$

where r_{ij} is the separation and where classically the parameter A_{ij} and ρ_{ij} are the size and hardness of the ion, respectively.

For the interactions between water molecules and HA surfaces we used the Buckingham potential parameters previously developed by de Leeuw [3], and between HA surfaces and the peptide a 6-12 Lennard Jones potential (eq. 2) from Generalised AMBER [4].

$$\Phi_{ij}\left(r_{ij}\right) = \frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^{6}} \quad (2)$$

where $A_{ij} = \sqrt{\varepsilon_i \varepsilon_j}\left(R_i + R_j\right)^{12}$ and $B_{ij} = 2\sqrt{\varepsilon_i \varepsilon_j}\left(R_i + R_j\right)^{6}$. In this function, $\left(R_i + R_j\right)$ is the minimum energy distance and $\sqrt{\varepsilon_i \varepsilon_j}$ the depth of the energy well.

Additional parameters used for the modelling of the interaction of the peptide with HA surfaces are report in Table S2.

Table S2 Additional non-bonded parameters

Van der Waals Parameters		
Atom type	R (Å)	ε (eV/23.0451mol)
Ca[5]	1.7131	0.4598
P	2.1000	0.2000
O2_SHL	1.6612	0.2100
O1_SHL	1.7210	0.2104
H1	0.0000	0.0000

Non-bonded parameters have been written in the DL_POLY format and units are *eV*.

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Ca	O2_SHL	buck	1550.0000	0.297	0
Ca	O1_SHL	buck	1250.0000	0.3437	0
Ca	OW	buck	1186.6000	0.297	0
H1	O2_SHL	buck	312.0000	0.25	0
H1	O1_SHL	buck	312.0000	0.25	0
H1	OW	buck	396.3000	0.25	0
O2_SHL	O2_SHL	buck	16372.0000	0.213	3.47
O2_SHL	OW	buck	22764.0000	0.149	17.14
O1_SHL	O1_SHL	buck	22764.0000	0.149	6.97
O1_SHL	OW	buck	12533.6000	0.213	12.09
O2_SHL	O1_SHL	buck	22764.0000	0.149	4.92
HW	O2_SHL	buck	396.3000	0.23	0
HW	O1_SHL	buck	312.0000	0.25	0
HW	OW	buck	396.3000	0.25	10
O	Ca	12-6	29377.4379	39.80538	
O	O2_SHL	12-6	16484.0146	24.51215	
O	O1_SHL	12-6	20438.2927	27.30731	
O	P	12-6	71279.1401	50.35399	
O	O	12-6	16484.0146	24.51215	
O	N	12-6	26328.8120	29.38293	
O	CA	12-6	28108.2489	27.19183	
O	C	12-6	24921.4175	24.1089	
O	Ha	12-6	1603.0455	3.996825	
O	H	12-6	44.5192	0.666107	
O	OD	12-6	20438.2927	27.30731	
O	CB	12-6	28108.2489	27.19183	
O	CG	12-6	28108.2489	27.19183	
O	CD	12-6	28108.2489	27.19183	
O	Hb	12-6	2661.4139	4.850966	
O	Hg	12-6	2661.4139	4.850966	
O	Hd	12-6	1603.0455	3.996825	
C	Ca	12-6	43856.6457	38.90651	
C	O2_SHL	12-6	24924.7128	24.11209	
C	O1_SHL	12-6	30453.4422	26.66518	
C	P	12-6	97795.1810	47.18252	
C	CA	12-6	40125.7487	25.9898	
C	C	12-6	35581.1140	23.0462	
C	N	12-6	37321.1162	27.98508	
C	Ha	12-6	2661.1327	4.080623	
C	H	12-6	98.7530	0.793624	
C	OD	12-6	30453.4422	26.66518	
C	CD	12-6	40125.7487	25.9898	
C	CG	12-6	40125.7487	25.9898	
C	CB	12-6	40125.7487	25.9898	
C	Hd	12-6	2661.1327	4.080623	
C	Hg	12-6	3738.0169	4.882391	
C	Hb	12-6	3738.0169	4.882391	
CA	CA	12-6	110300.3499	53.2158	

CA	N	12-6	43191.4330	31.97259
CA	H	12-6	111.3806	0.895105
CA	Ha	12-6	2945.3995	4.60266
CA	Ca	12-6	49464.6394	43.88153
CA	O2_SHL	12-6	28111.8610	27.19533
CA	O1_SHL	12-6	34347.5547	30.07489
CA	P	12-6	110300.3499	53.2158
CA	OD	12-6	34347.5547	30.07489
CA	CD	12-6	45256.6689	29.31314
CA	CG	12-6	45256.6689	29.31314
CA	CB	12-6	45256.6689	29.31314
CA	Hd	12-6	2945.0209	4.602416
CA	Hg	12-6	154.8153	1.055234
CA	Hb	12-6	154.8153	1.055234
CD	OD	12-6	34347.5547	30.07489
CD	CD	12-6	45256.6689	29.31314
CD	CG	12-6	45256.6689	29.31314
CD	CB	12-6	45256.6689	29.31314
CD	N	12-6	43191.4330	31.97259
CD	Ha	12-6	2945.0209	4.602416
CD	Hd	12-6	2945.0209	4.602416
CD	Hg	12-6	154.8153	1.055234
CD	Hb	12-6	154.8153	1.055234
CD	H	12-6	111.3806	0.895105
CD	Ca	12-6	49464.6394	43.88153
CD	O2_SHL	12-6	28111.8610	27.19533
CD	O1_SHL	12-6	34347.5547	30.07489
CD	P	12-6	110300.3499	53.2158
CG	OD	12-6	34347.5547	30.07489
CG	CG	12-6	45256.6689	29.31314
CG	CB	12-6	45256.6689	29.31314
CG	N	12-6	43191.4330	31.97259
CG	Ha	12-6	2945.0209	4.602416
CG	Hd	12-6	2945.0209	4.602416
CG	Hg	12-6	154.8153	1.055234
CG	Hb	12-6	154.8153	1.055234
CG	H	12-6	111.3806	0.895105
CG	Ca	12-6	49464.6394	43.88153
CG	O2_SHL	12-6	28111.8610	27.19533
CG	O1_SHL	12-6	34347.5547	30.07489
CG	P	12-6	110300.3499	53.2158
CB	OD	12-6	34347.5547	30.07489
CB	CB	12-6	45256.6689	29.31314
CB	N	12-6	43191.4330	31.97259
CB	Ha	12-6	2945.0209	4.602416
CB	Hd	12-6	2945.0209	4.602416
CB	Hg	12-6	154.8153	1.055234
CB	Hb	12-6	154.8153	1.055234
CB	H	12-6	111.3806	0.895105
CB	Ca	12-6	49464.6394	43.88153
CB	O2_SHL	12-6	28111.8610	27.19533
CB	O1_SHL	12-6	34347.5547	30.07489
CB	P	12-6	110300.3499	53.2158
N	N	12-6	2905.0809	6.54537

N	Ha	12-6	2692.9161	4.913727
N	H	12-6	92.2543	0.909538
N	Ca	12-6	46525.6539	47.51584
N	O2_SHL	12-6	26332.2063	29.38671
N	O1_SHL	12-6	32326.8122	32.57583
N	P	12-6	106637.0495	58.42035
N	OD	12-6	32326.8122	32.57583
N	Hd	12-6	2692.9161	4.913727
N	Hg	12-6	3890.8933	5.906419
N	Hb	12-6	3890.8933	5.906419
Ha	Ca	12-6	2905.0809	6.54537
Ha	O2_SHL	12-6	1603.2515	3.99734
Ha	O1_SHL	12-6	2026.1215	4.49583
Ha	P	12-6	7857.9429	8.74233
Ha	Ha	12-6	216.3245	0.767742
Ha	H	12-6	2.5804	0.083857
Ha	Hd	12-6	216.3245	0.767742
Ha	Hg	12-6	216.3245	0.767742
Ha	Hb	12-6	216.3245	0.767742
Hd	Hd	12-6	216.3245	0.767742
Hd	Hg	12-6	216.3245	0.767742
Hd	Hb	12-6	216.3245	0.767742
Hd	H	12-6	2.5804	0.083857
Hd	Ca	12-6	2905.0809	6.54537
Hd	O2_SHL	12-6	1603.2515	3.99734
Hd	O1_SHL	12-6	2026.1215	4.49583
Hd	P	12-6	7857.9429	8.74233
Hg	Hg	12-6	216.3245	0.767742
Hg	Hb	12-6	216.3245	0.767742
Hg	H	12-6	2.5804	0.083857
Hg	Ca	12-6	2905.0809	6.54537
Hg	O2_SHL	12-6	1603.2515	3.99734
Hg	O1_SHL	12-6	2026.1215	4.49583
Hg	P	12-6	7857.9429	8.74233
Hb	Ca	12-6	4252.1873	7.91883
Hb	O2_SHL	12-6	2361.7174	4.85159
Hb	O1_SHL	12-6	2962.8229	5.43663
Hb	P	12-6	11032.1973	10.35866
Hb	Hb	12-6	216.3245	0.767742
Hb	H	12-6	2.5804	0.083857
OD	OD	12-6	25246.2457	30.36418
OD	H	12-6	60.9530	0.77978
OD	Ca	12-6	36305.9733	44.27213
OD	O2_SHL	12-6	20438.2927	27.30731
OD	O1_SHL	12-6	25246.2457	30.36418
OD	P	12-6	86215.0323	55.40523
H	Ca	12-6	86.4934	1.1294
H	O2_SHL	12-6	44.5193	0.66611
H	O1_SHL	12-6	60.9530	0.77978
H	P	12-6	364.9645	1.88407
H	H	12-6	0.0061	0.00407
OW	O	12-6	77698.6918	95.51224
OW	C	12-6	30212.8448	24.47688
OW	CA	12-6	34076.1904	27.60676

OW	N	12-6	32188.9421	29.95719
OW	CB	12-6	34076.1904	27.60676
OW	CG	12-6	34076.1904	27.60676
OW	CD	12-6	34076.1904	27.60676
OW	Ha	12-6	2062.7605	4.180564
OW	Hb	12-6	2999.5295	5.041237
OW	Hd	12-6	2062.7605	4.180564
OW	Hg	12-6	2062.7605	4.180564
OW	OW	12-6	25232.7276	25.79161
OW	H	12-6	65.9480	0.3138999
OW	OD	12-6	25257.6900	27.98941
P	OW	12-6	84937.4546	50.70005

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1. G. W. Watson, E. T. Kelsey, N. H. deLeeuw, D. J. Harris and S. C. Parker, *J Chem Soc Faraday T*, 1996, **92**, 433-438.
2. A. Wierzbicki and H. S. Cheung, *J Mol Struc-Theochem*, 2000, **529**, 73-82.
3. N. H. de Leeuw, *Phys Chem Chem Phys*, 2004, **6**, 1860-1866.
4. W. D. Cornell, P. Cieplak, C. I. Bayly, I. R. Gould, K. M. Merz, D. M. Ferguson, D. C. Spellmeyer, T. Fox, J. W. Caldwell and P. A. Kollman, *Journal of the American Chemical Society*, 1995, **117**, 5179-5197.
5. J. Robinson, I. Cukrowski and H. M. Marques, *Journal of Molecular Structure*, 2006, **825**, 134-142.