Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Electronic Supplementary Information for **Computer Simulations of N-terminal Peptide of Statherin, SN15 and Its Mutants Adsorption on Hydroxyapatite Surfaces**

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Table S1: Full sequences of SN series peptides.

Peptide	Sequence	Note
SN15	D-pS-pS-EEKFLRRIGRFG	pS denotes phosphoserines
SN_S15	DSSEEKFLRRIGRFG	S denotes serine
SN_A15	DDDEEKFLRRIGRFG	D denotes aspartic acid

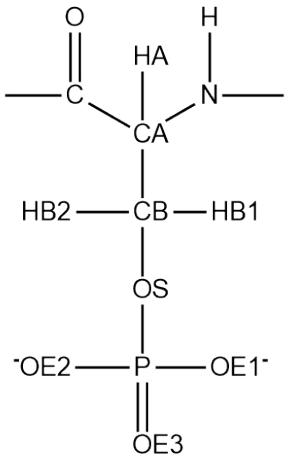

Figure S1: Structure and atom names of phosphoserines. The atom names, bonds, angles and dihedrals were used corresponding to the Amber99sb-ildn parameter set.

Table S2: Atom types and partial charges of each atom in phosphoserines, adopted from the reference.[1]

Atom name	Atom type	Charge
C	C	0.557437
O	O	-0.629560
CA	CT	-0.278702
HA	H1	0.198553
CB	CT	0.253803
HB1	H1	0.043230
HB2	H1	0.043230
OS	OS	-0.430343
P	P	1.387087
OE1	O2	-0.982953
OE2	O2	-0.982953
OE3	O2	-0.982953
N	N	-0.481860
H	H	0.285984

The HAP force field parameters used in this work was developed by Hauptmann et al[2]. This force field reproduced the experimental bulk crystal parameters with high accuracy (e.g., within less than 1% deviation for a wide range of temperatures between 73 and 1273K)[2]; therefore, the force field has been adopted extensively in various HAP-simulation studies[3-7]. In Hauptmann et al.'s original formulation, the intermolecular interactions between the ionic groups in HAP was described as a summation of Coulombic and Born-Mayer-Huggins (BMH) potentials for electrostatic and van der Waals interactions. In our previous work, we have fitted it into Lennard-Jones potential (see Table S3) to be compatible with GROMACS' force field[3]. These force field parameters has been evaluated by our previous work[3]. Here, we also reevaluated them through MD simulation in NPT ensemble.

The system contains 4×3×5 HAP crystal units in a periodic box. Cutoff distance of 1.3 nm was adopted for short-range non-bonded forces. Bonds were constrained by the LINCS algorithm[8]. Particle Mesh Ewald (PME)[9], V-rescale[10] and Parrinello-Rahman[11] methods were used. The simulation ran 3 ns in NPT ensemble. At 310 K, the Lennard-Jones parameters provide a bulk crystal lattice parameters average deviation of 0.8% (see Table S4), which means that the force field well reproduces the structure properties of HAP.

Table S3: Partial charges[2] and VDW parameters[12] for HAP surface.

Atom	Charge (e)	ε (kJ·mol-1)	σ (nm)
Ca	+2.0	0.49635	0.29413
P	+2.6	4.07547	0.34857
O (P)	-1.4	1.05441	0.30325
O (H)	-1.6	0.48965	0.30929
H	+0.6	0.00004	0.14042

Table S4: Simulated and experimental[13] HAP unit cell parameters at 310K.

	a (nm)	b (nm)	c (nm)	α	β	γ
Simulation	0.9351	0.9351	0.6830	90	90	120
Experimental	0.9423	0.9423	0.6883	90	90	120

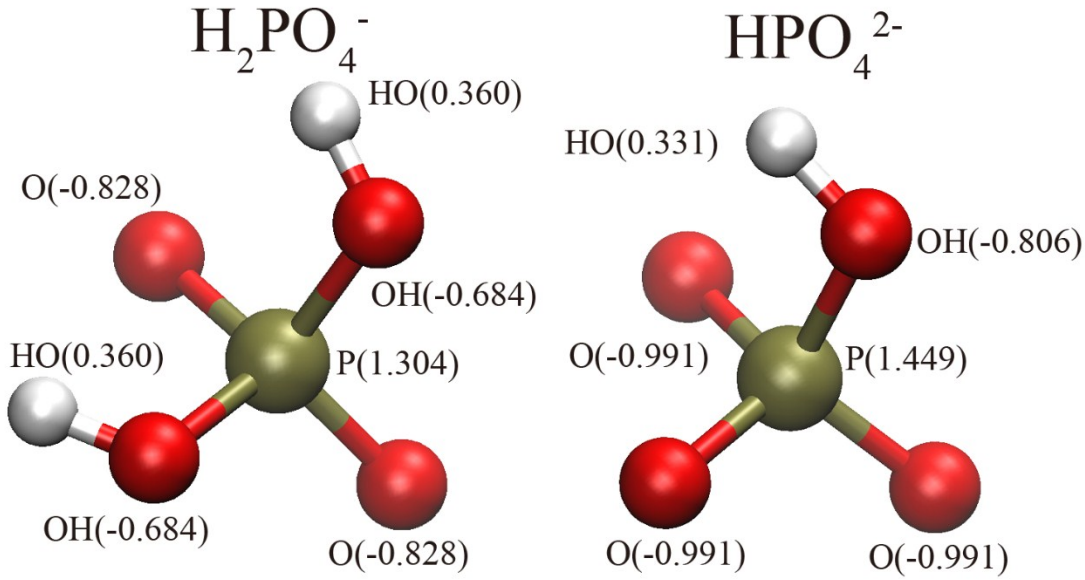

Figure S2: Amber99sb-ildn atom types and fractional charges assigned to each atom in phosphate ions. The charges are obtained from a structure optimized in gas phase at the HF/6-31G* level; atoms of the same type are restrained to have identical charges. Charge assignment for dihydrogen phosphate is adopted from reference.[14] The atom type, bonds, angles and dihedrals were taken from existing parameters in the Amber99sb-ildn force filed.

Table S5: Setting for all simulated systems.

Peptide	Solution environment	Ca^{2+} (M)	$H_2PO_4^-$ /HPO_4^{2-} (M)	Na^+/Cl^- (M)	No. of water molecules
SN15	NaCl	0	0/0	13/10 (0.12)	3286
	Ca/P	10 (0.12)	3/3 (0.072)	0/8 (0)	3308
SN_A15	NaCl	0	0/0	11/10 (0.12)	3288
	Ca/P	10 (0.12)	3/3 (0.072)	0/10 (0)	3310
SN_S15	NaCl	0	0/0	10/11 (0.12)	3287
	Ca/P	10 (0.12)	3/3 (0.072)	0/12 (0)	3315

An orientation angle (θ) was applied to quantitatively characterize the orientation of adsorbed peptides on HAP surfaces, as revealed in Fig.S3, which is defined as the angle between the unit vector along the dipole of a protein and a vector perpendicular to the HAP surface and passing through the centre of mass of the peptide according to our previous work[3, 15, 16]. We've calculated the cosine value of this angle (cos θ) to represent the orientation of adsorbed peptides, which has been illustrated in Fig. S4.

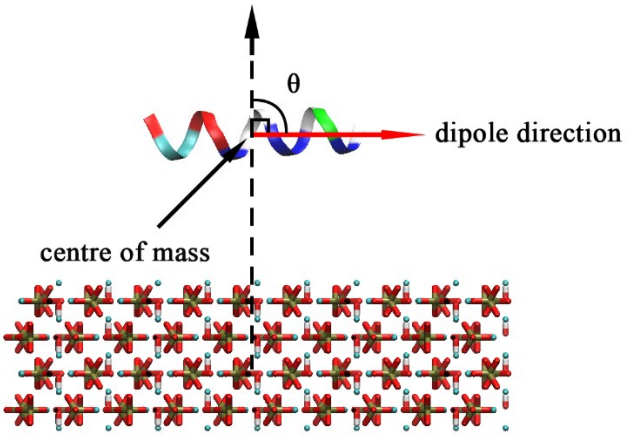

Fig. S3: The definition of orientation of peptide among the HAP surface. θ is the angle between the unit vector along the dipole of a protein and a vector perpendicular to the HAP surface and passing through the centre of mass of the peptide.

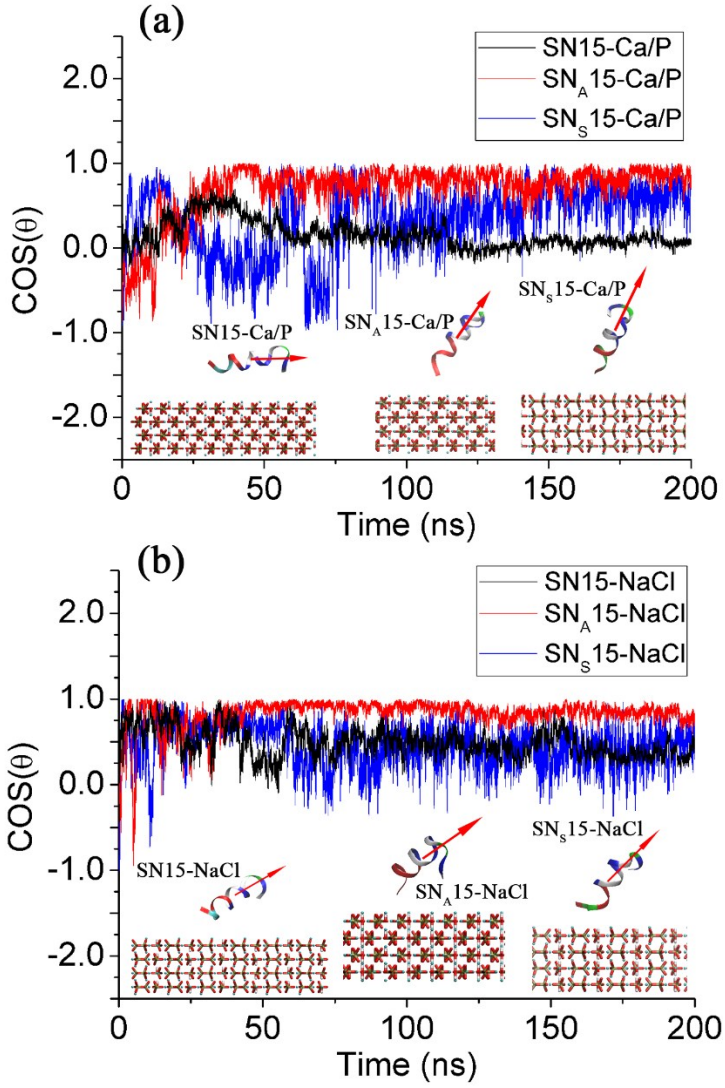

Fig. S4: Orientation of three kinds of peptides in (a) Ca/P solution and (b) NaCl solution. Insets: Illustration of the orientation of each system.

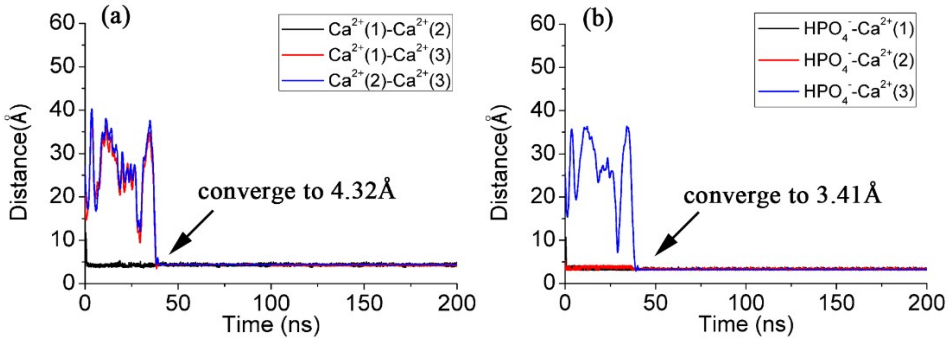

Fig. S5: We named three calcium ions that involved in "(Sep3-PO_4^{2-})-3Ca^{2+}-HPO_4^- structure" as Ca^{2+}(1), Ca^{2+}(2) and Ca^{2+}(3), then we calculated (a) the distance between 3 Ca^{2+} ions, and (b) the distance between HPO_4^- ions and them. As can be seen, each distance has converged.

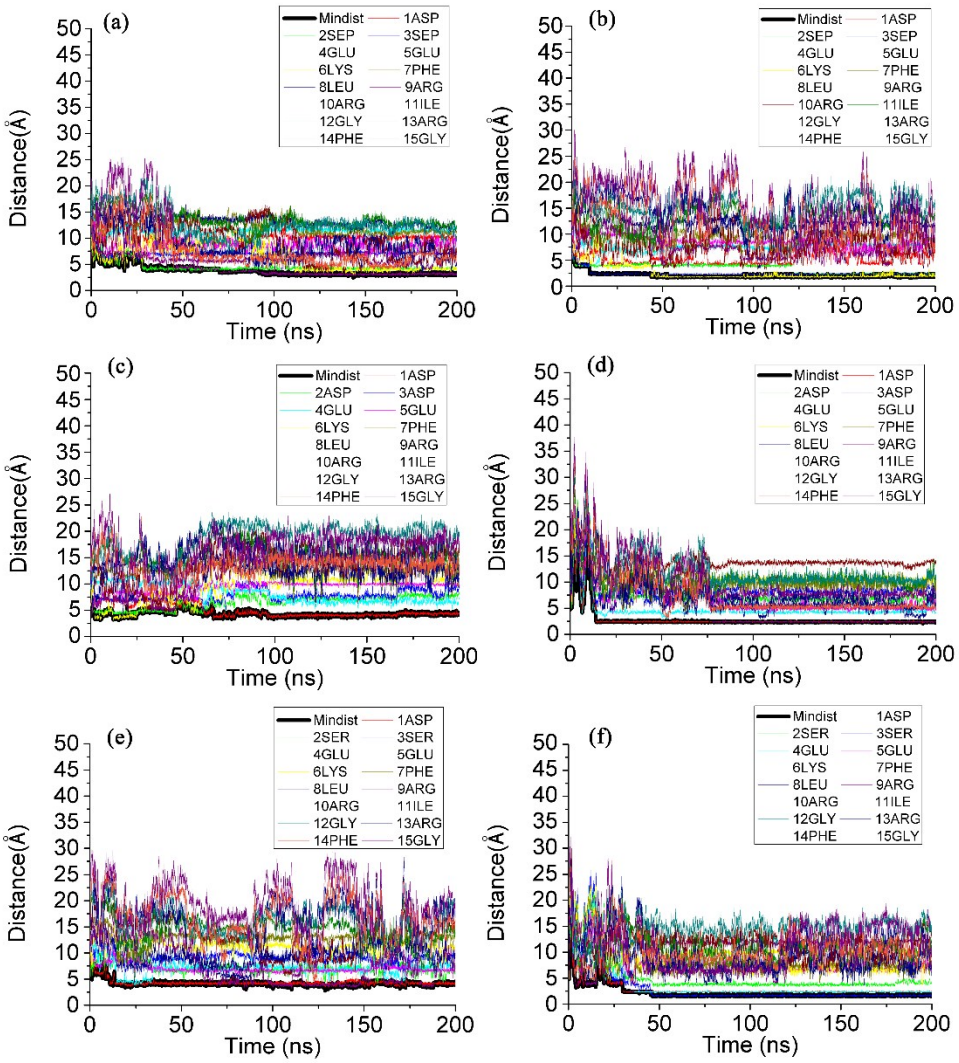

Fig. S6: Minimum distance for (a) SN15 peptide in Ca/P solution, (b) SN15 peptide in NaCl solution, (c) SN_A15 peptide in Ca/P solution, (d) SN_A15 peptide in NaCl solution, (e) SN_S15 peptide in Ca/P solution and (f) SN_S15 peptide in NaCl solution and their each amino acid to the HAP surface.

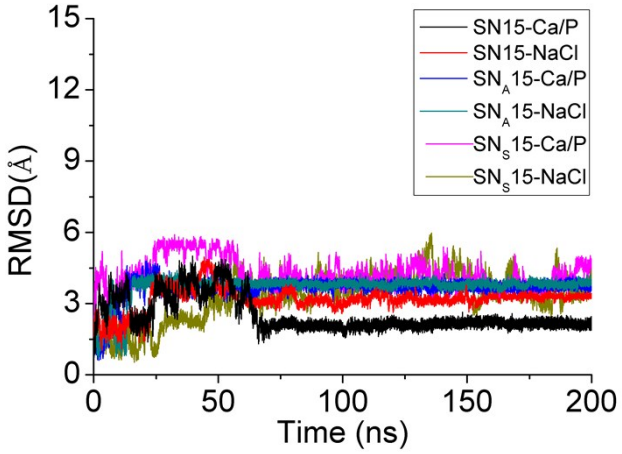

Fig. S7: Backbone RMSD function of three peptides in Ca/P and NaCl solutions during 200 ns simulations.

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