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

Supporting Information

Computational study on Strontium ion modified Hydroxyapatite-Fibronectin interaction

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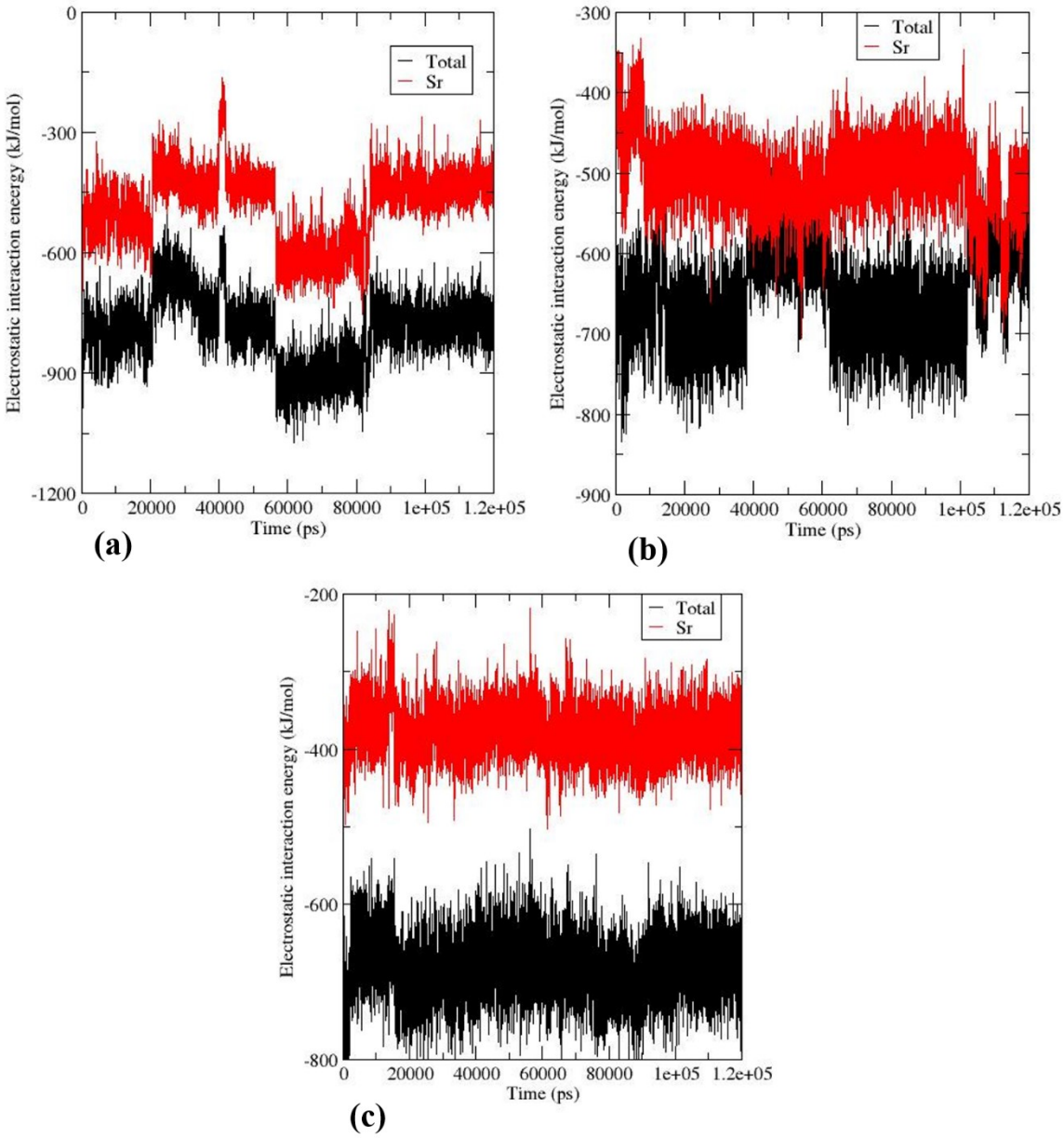


Fig S1: Comparison of total electrostatic interaction between FN and surface with that between Sr^{2+} and FN for (a)10SrHA, (b)20SrHA, and (c) 30SrHA.

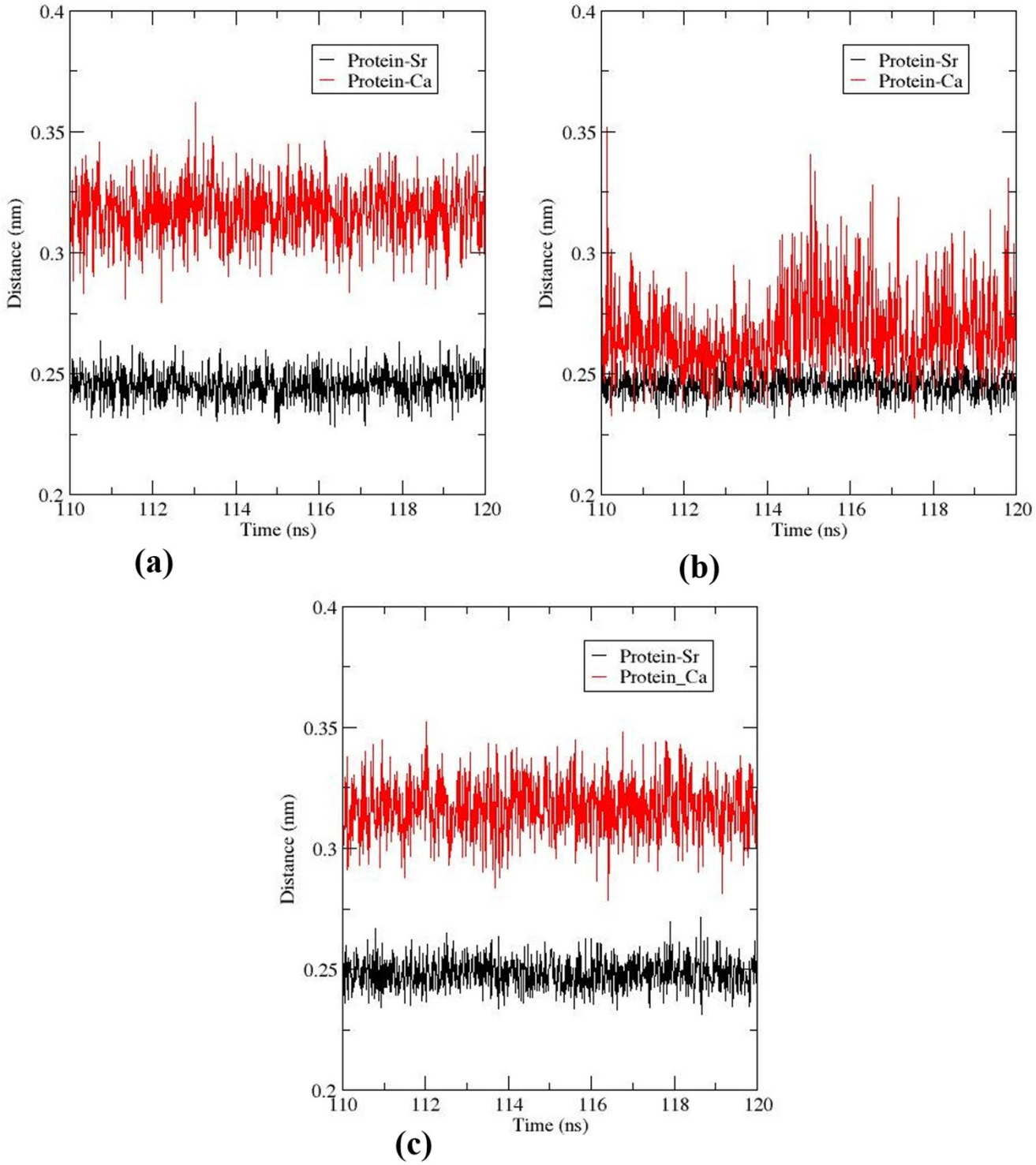


Fig S2: Comparison of minimum distances between FN and Ca^{2+} with that between FN and Sr^{2+} for (a)10SrHA, (b)20SrHA, and (c) 30SrHA.

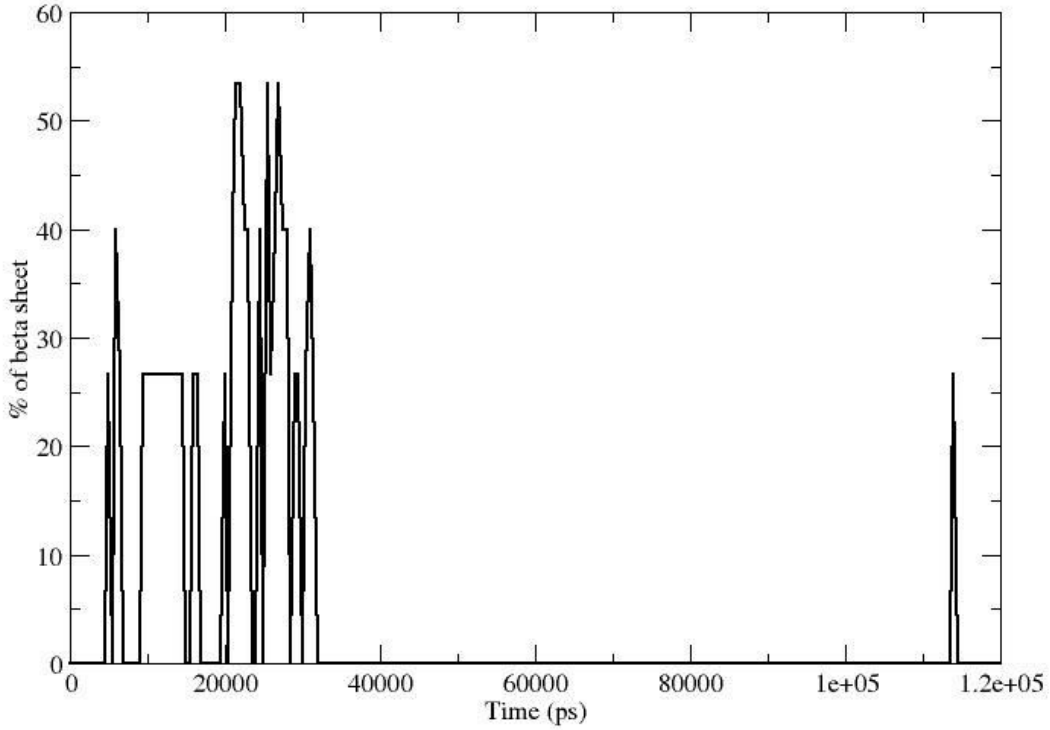


Fig S3: Temporal evolution of percentage of β-sheet in 'area2' (residue74-88) of FN.

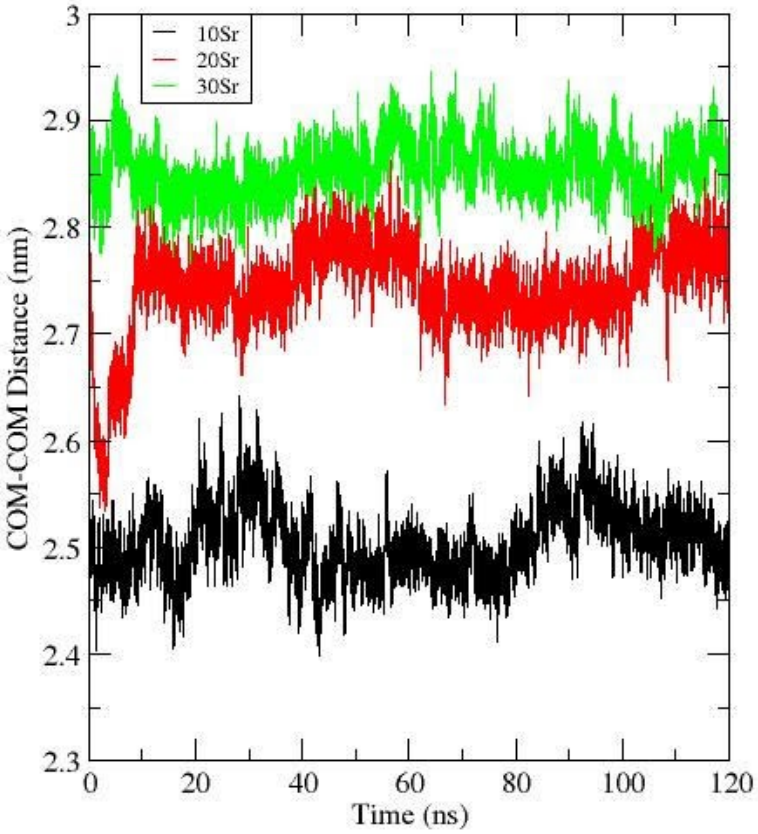


Fig S4: COM-COM distance between FN and Sr^{2+} ions. Increasing distance indicates Sr^{2+} ions were substituted away from FN module.

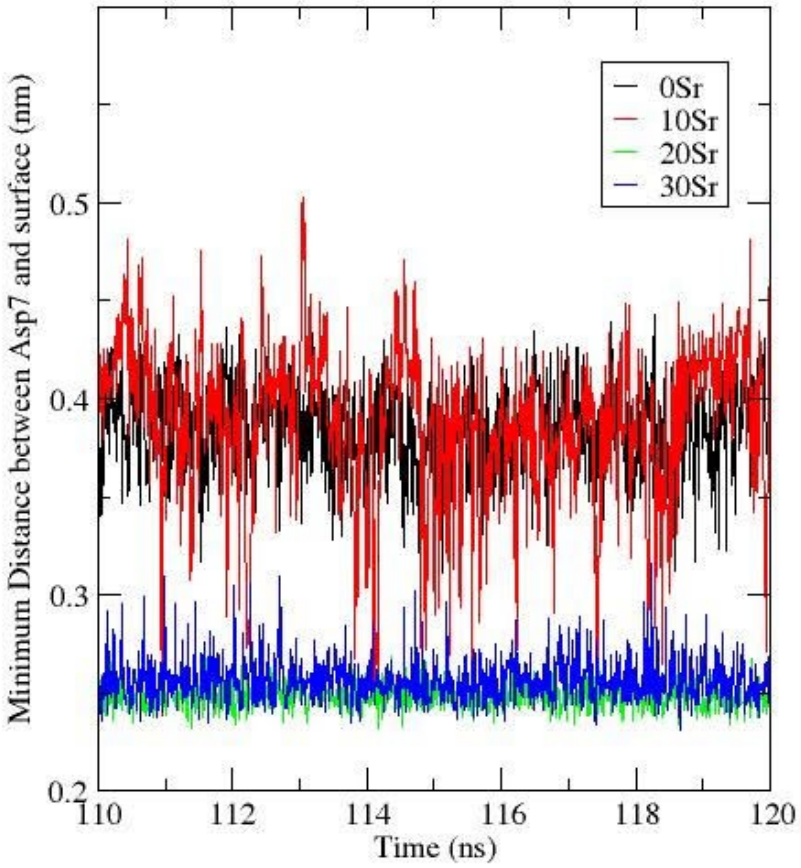
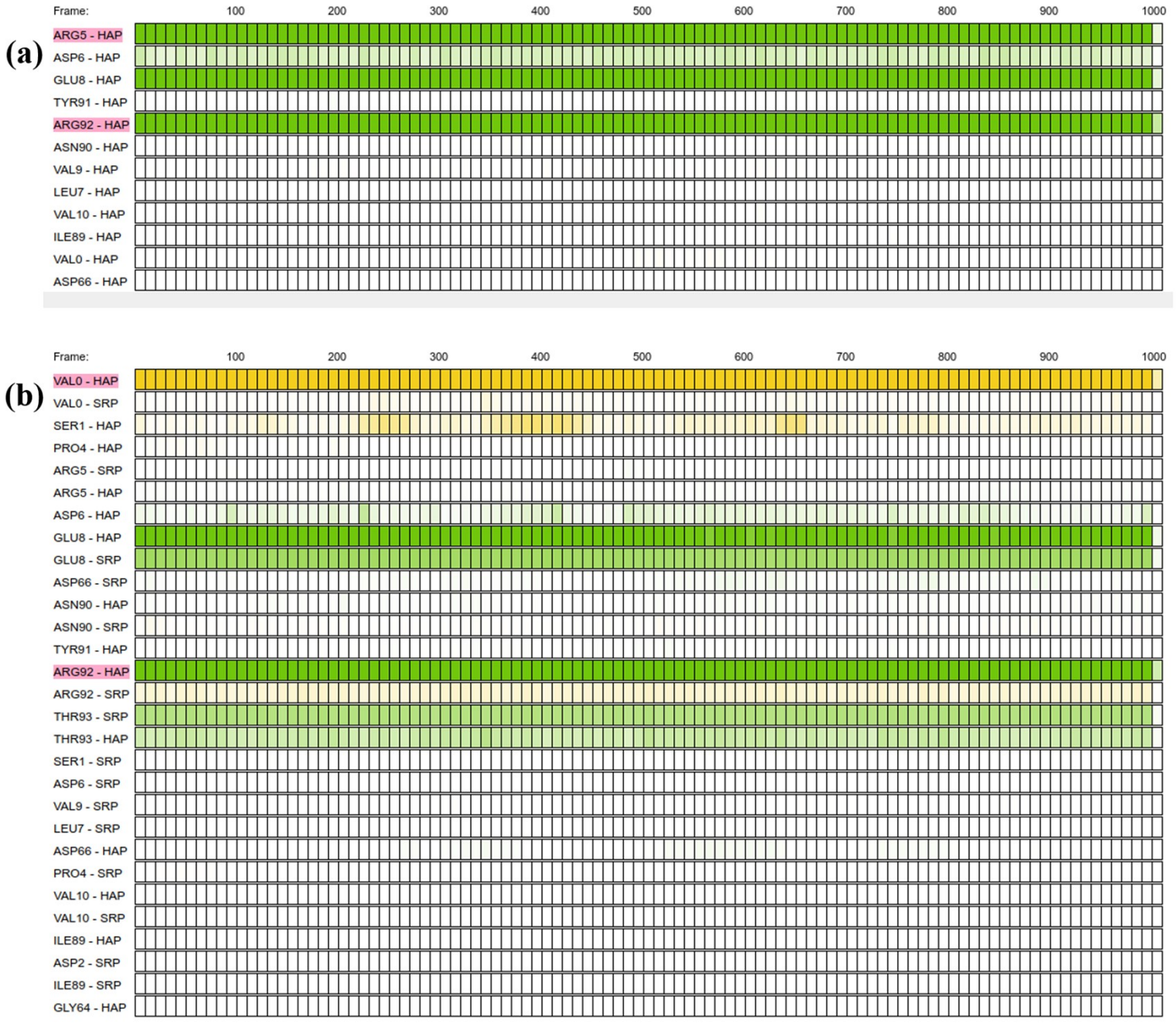


Fig S5: Minimum distance between Asp7 residue and undoped/Sr-doped HA surfaces.


(a)
Frame:
100
200
300
400
500
600
700
800
900
1000
ARG5 - HAP
ASP6 - HAP
GLU8 - HAP
TYR91 - HAP
ARG92 - HAP
ASN90 - HAP
VAL9 - HAP
LEU7 - HAP
VAL10 - HAP
ILE89 - HAP
VAL0 - HAP
ASP66 - HAP
(b)
Frame:
100
200
300
400
500
600
700
800
900
1000
VAL0 - HAP
VAL0 - SRP
SER1 - HAP
PRO4 - HAP
ARG5 - SRP
ARG5 - HAP
ASP6 - HAP
GLU8 - HAP
GLU8 - SRP
ASP66 - SRP
ASN90 - HAP
ASN90 - SRP
TYR91 - HAP
ARG92 - HAP
ARG92 - SRP
THR93 - SRP
THR93 - HAP
SER1 - SRP
ASP6 - SRP
VAL9 - SRP
LEU7 - SRP
ASP66 - HAP
PRO4 - SRP
VAL10 - HAP
VAL10 - SRP
ILE89 - HAP
ASP2 - SRP
ILE89 - SRP
GLY64 - HAP

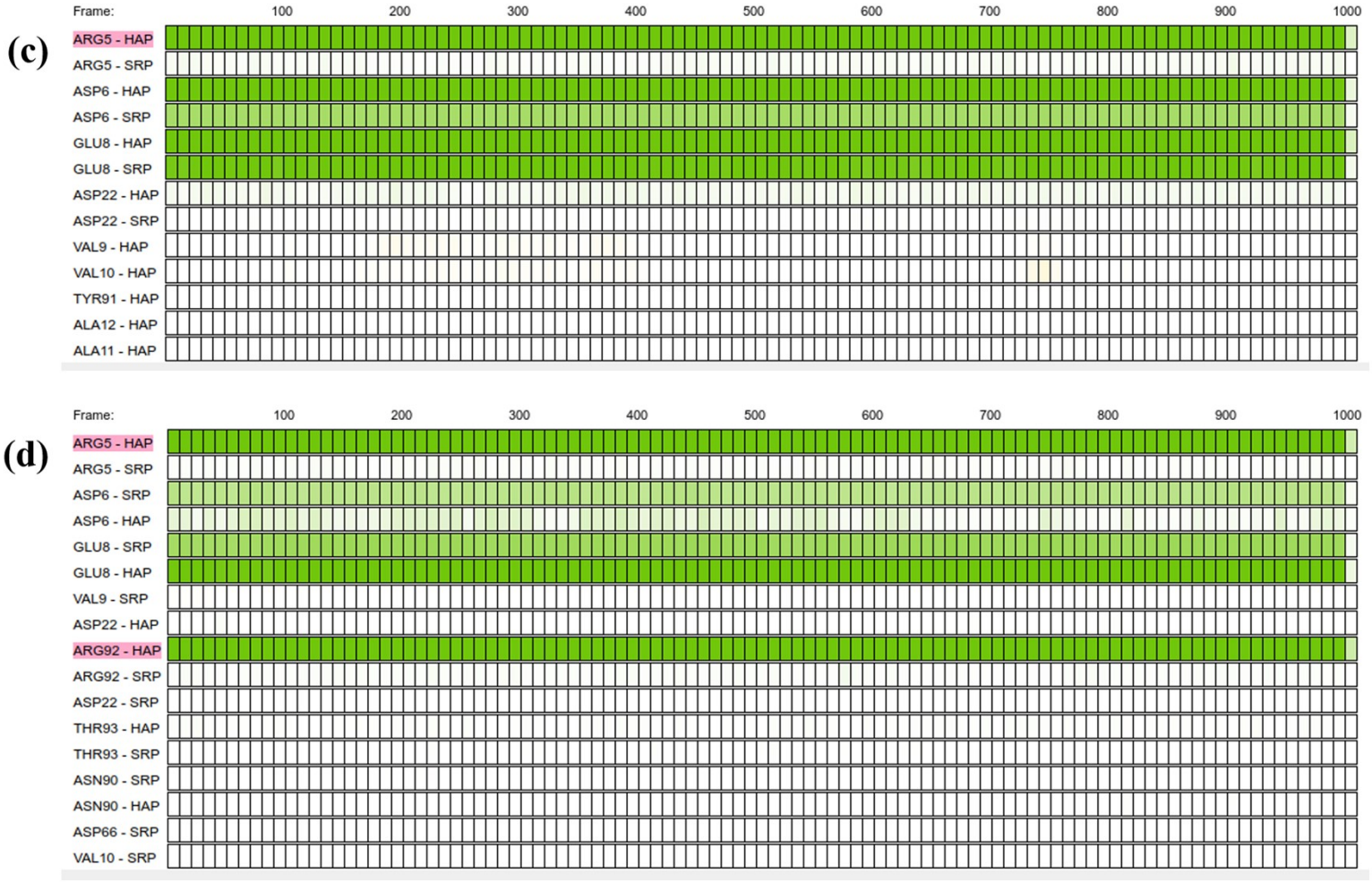


Fig S6: Timeline of the contact analysis of the last 1000 frames (110-120 ns) of the simulation for (a)0SrHA, (b) 10SrHA, (c) 20SrHA, and (d) 30SrHA, obtained using PyContact tool.[1] Pink colour at the left most panels highlights hydrogen bond forming residues. Green and yellow colour indicates side chain-side chain and side chain-backbone interactions, respectively. Strength of the interaction is proportional to the colour intensity. Cut off distance for the analysis was 5Å.

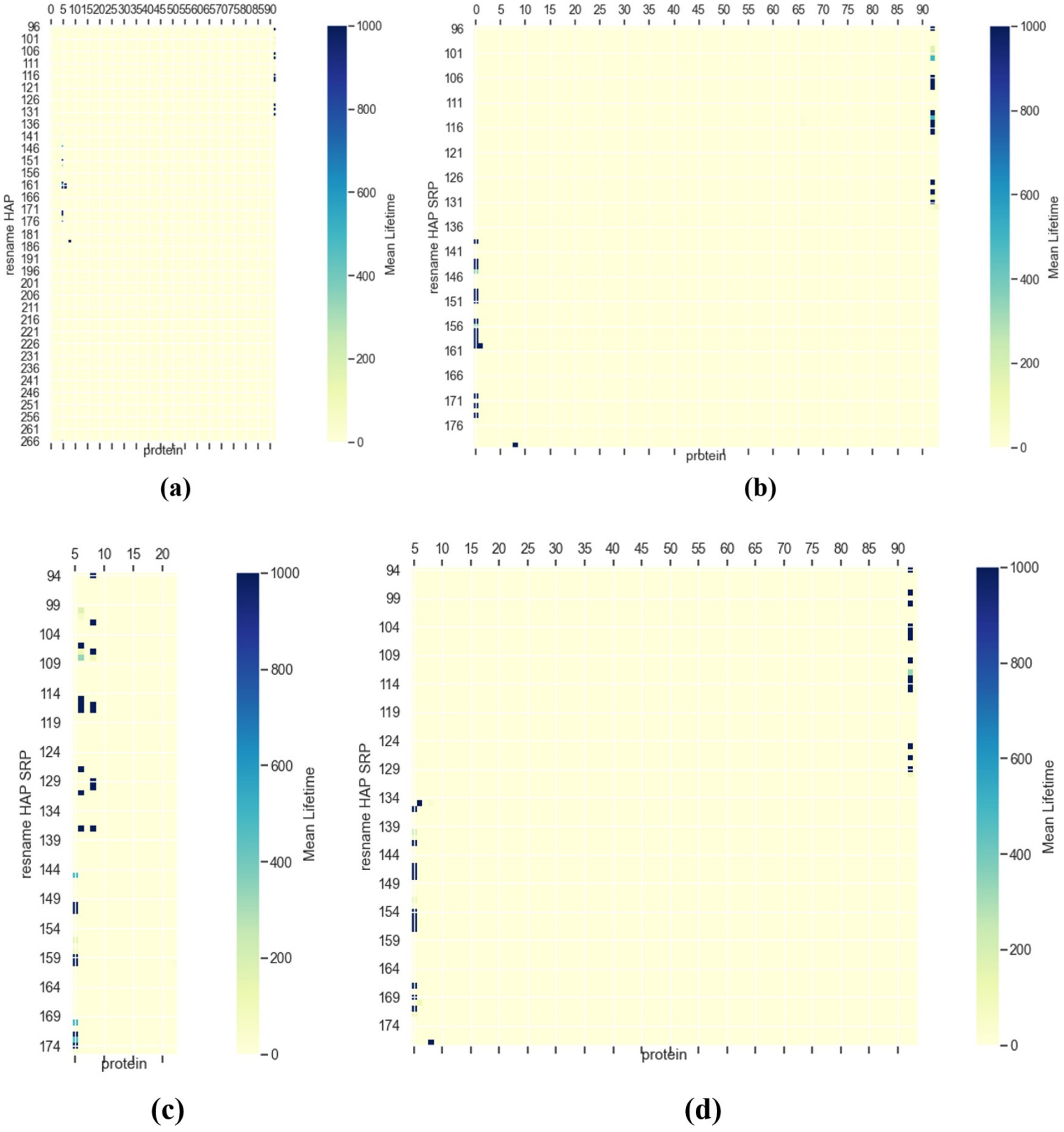


Fig S7: FN-materials surface Contact map for (a)0SrHA, (b) 10SrHA, (c) 20SrHA, and (d) 30SrHA, obtained using PyContact tool.[1] A contact has been formed when two atoms, one from FN and other from the surface are within a distance of 5Å. The mean life time (a.u) of the contacts formed between residues of FN and surface is estimated and shown.

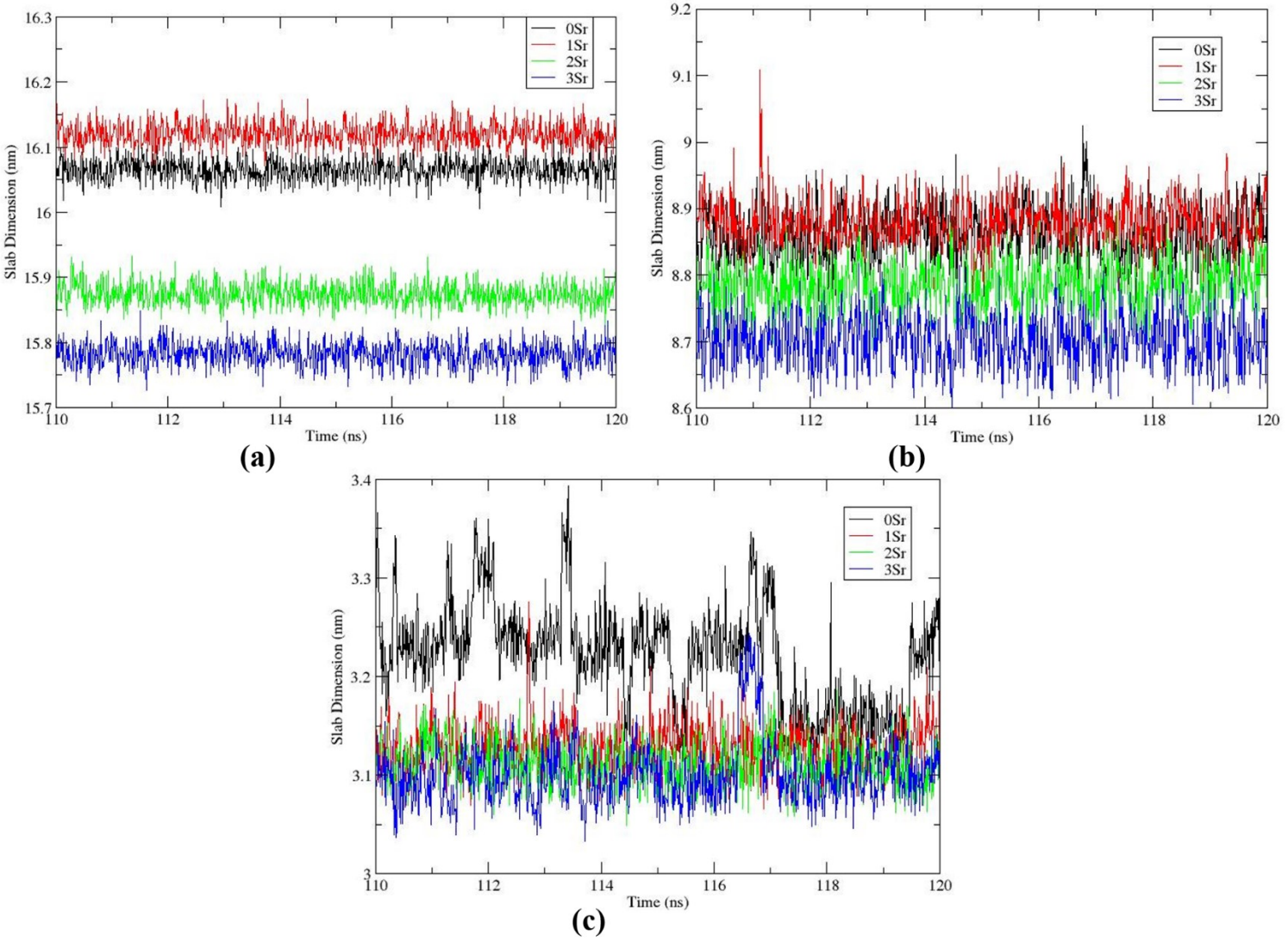
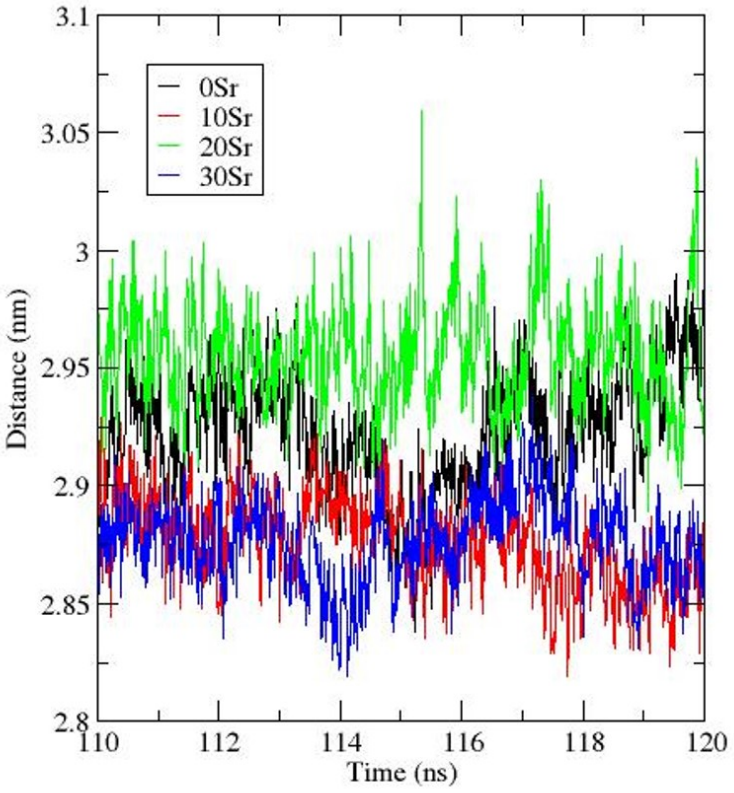
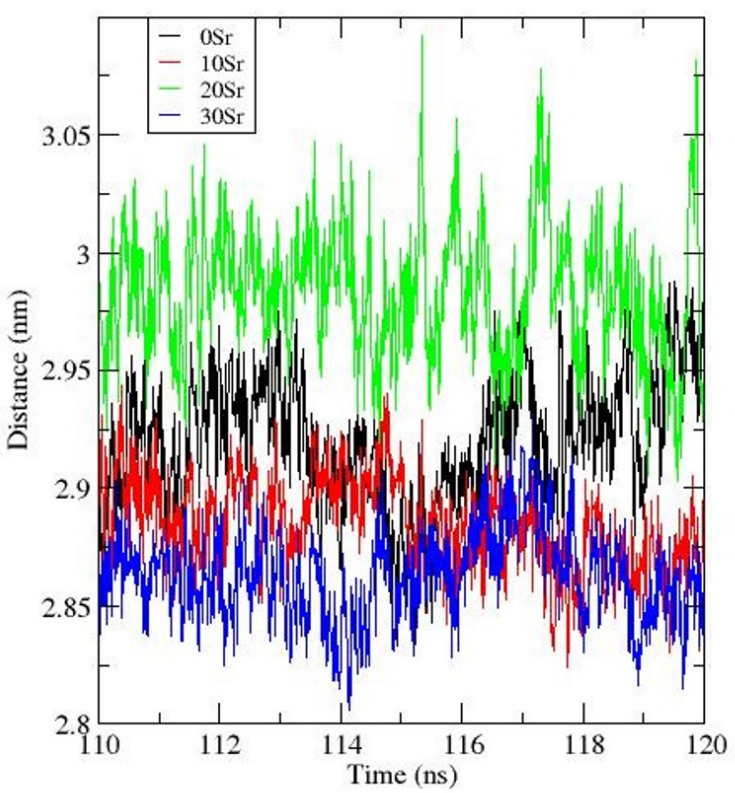


Fig S8: Doping dependent change in the material slab size along (a) x, (b)y, and (c)z axis. Sample designation: xSr: 10x mol% Sr^{2+}-doped HA.



(a)



(b)

Fig S9: COM-COM distance between FN and (a) PO_4^{3-} , and (b)OH^- group.

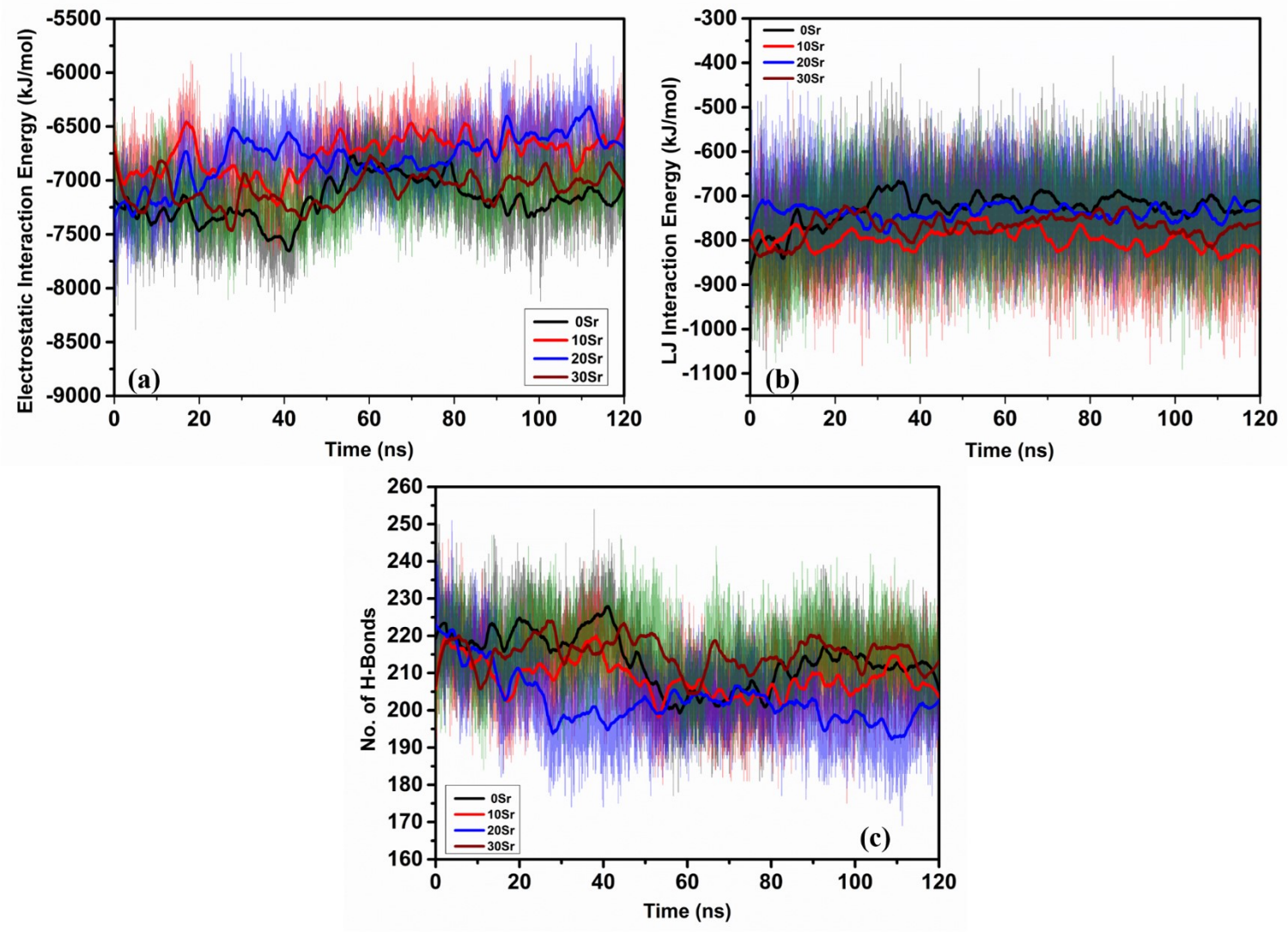
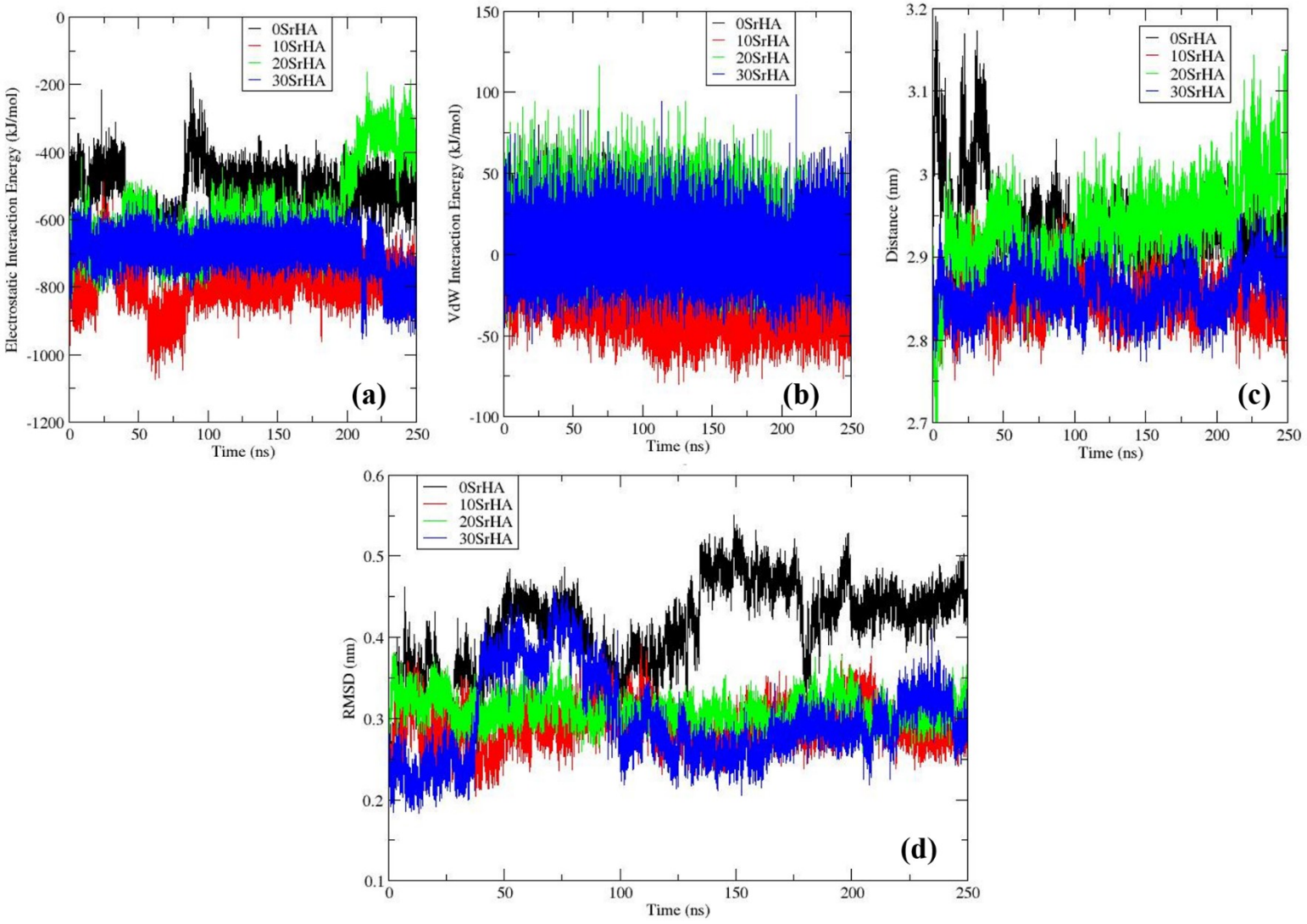


Fig S10: (a) Coulombic, and (b)LJ interaction between FN and water in presence of different Sr-doped HA surface. (c) Number of Hydrogen bonds formed between water and FN.



Long-term effect of Strontium on FN adsorption

Fig. S11: Temporal evolution of (a) FN-(Sr-doped) HA coulombic interaction energy, (b) FN-(Sr-doped) HA VdW interaction energy, (c) FN-(Sr-doped) HA COM-COM distance, and (d) RMSD of FN backbone. Sample designation: xSrHA means x mol% Sr^{2+} -doped hydroxyapatite.

Additional runs for 130ns (total 250ns) have been performed to observe the long-term effects of Sr-doping inside HA structures on FN adsorption, and the calculated quantities have been depicted in Fig. S11. Fig. S11(a) and (b) present electrostatic and VdW interaction energies between the FN and pure/Sr-doped HA. As mentioned earlier, the adsorption phenomena were driven by the coulombic interaction, and the highest interaction energy was observed for

10SrHA, for most of the simulation window (Fig. S11(a)). After 200ns, the interaction energy between FN and 30SrHA was almost identical to that between FN and10SrHA (Fig. S11(a)). This implies that, at a longer time scale, the adsorption capacity of 30SrHA will become equivalent to that of 10SrHA. However, a faster stabilization of adsorbed FN on 10SrHA surface can be seen from the steady interaction energy and COM-COM distance between FN and biomaterials surface (Fig. S11(a) and S11(c)). This establishes the fact that.10SrHA is the most suitable substrate for FN adsorption.

All Sr-doped HA outperformed pure HA surface in terms of protein-surface interaction, for most of the simulation time (Fig. S11(a)). A notable exception is that the attractive coulombic interaction between 20SrHA and FN was less than that between 0SrHA and FN between 200ns and 250ns (Fig. 11(a)). This indicates that there exists an optimum window for Sr content inside the apatite structure, where adsorption capacity becomes maximum.

LJ interactions between FN and different Sr-doped HA (0 0 1) surfaces have been presented in Fig. S11(b). No significant change is found in protein-surface LJ interaction with surface modification. The COM-COM distance between FN and biomaterials slabs is shown in Fig. S11 (c), and a steady adsorbed state of FN on every biomaterial surface can easily be interpreted. Besides this, the better stability of FN on Sr-doped HA surfaces compared to undoped HA can be observed in Fig. S11(d).

References

1 M. Scheurer, P. Rodenkirch, M. Siggel, R. C. Bernardi, K. Schulten, E. Tajkhorshid and T. Rudack, PyContact: rapid, customizable, and visual analysis of noncovalent interactions in MD simulations, *Biophys. J.*, 2018, **114**, 577–583.