# Electronic Supplementary Information

## A Combined DFT and MD Simulation Studies of Protein Stability on Imidazolium-Water Clusters ($ImH^+W_n$) with Aromatic Amino Acids‡

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Percentage of reduction BEs, noncovalent index (NCI) plots of AAs-$ImH^+W_n$ (n = 1 – 3) clusters, SDF and potential energy plots of Protein-L with AAs are obtained from MD simulations provided in this supporting information.

The overall reduction percentages of BEs are 50%, 66%, and 75 % for the Phe-$ImH^+W_4$, Trp-$ImH^+W_4$ and Tyr-$ImH^+W_4$, respectively. The percentage of reduction in the BE plot is displayed in **Fig. S1**. From that, water molecules considerably decrease the interaction affinity of hydrophobic AAs (i.e., Phe) when compare with the Trp and Tyr. A very less reduction of BEs observed in Trp and Tyr, because of the formation of π stacking with water-mediated H-bonds. The water-mediated H-bonded networks are playing a main driving force for the stability of π-stacking complexes.

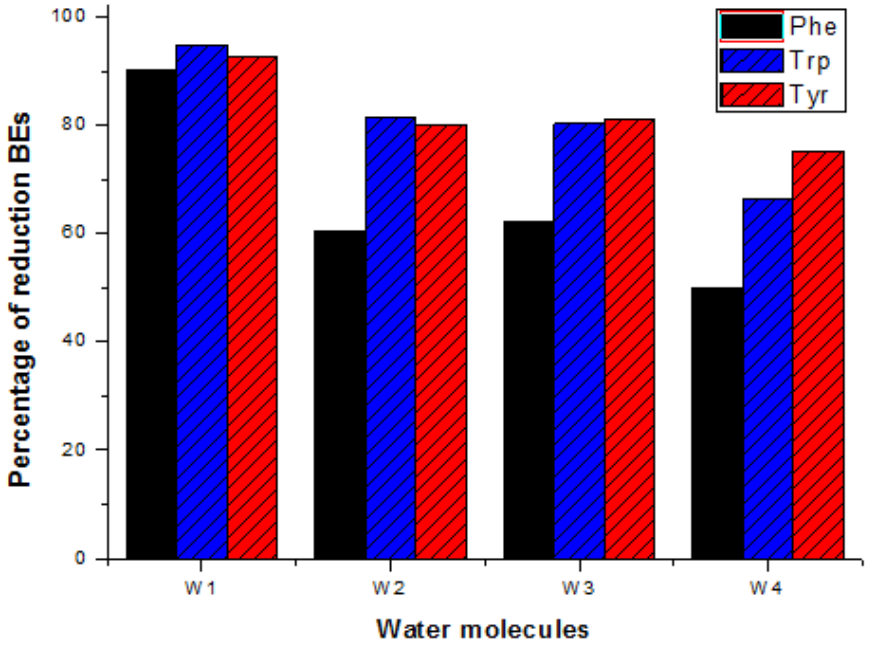
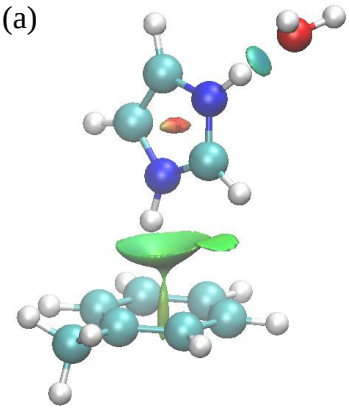
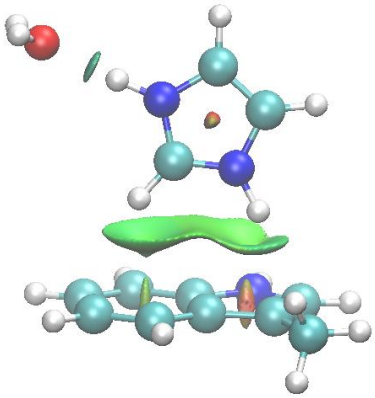



**Fig. S1** The percentage of reduction of BEs during the stepwise addition of water molecules with AAs (Phe, Trp, and Tyr). W1, W2, W3, and W4 are denoted as AAs-$ImH^+$ with water monomer, dimer, trimer, and tetramer, respectively.

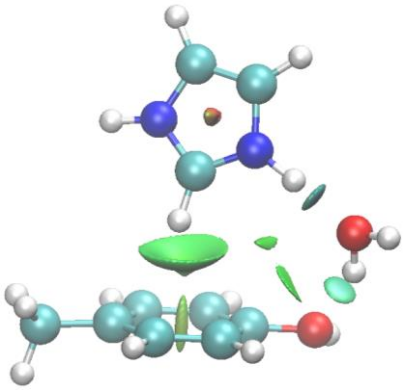
(a)



Phe-ImH$^+$w$_1$

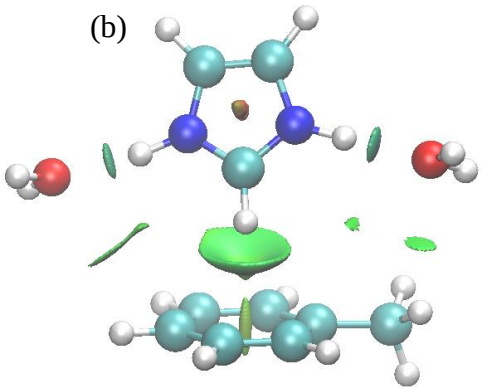


Trp-ImH$^+$w$_1$

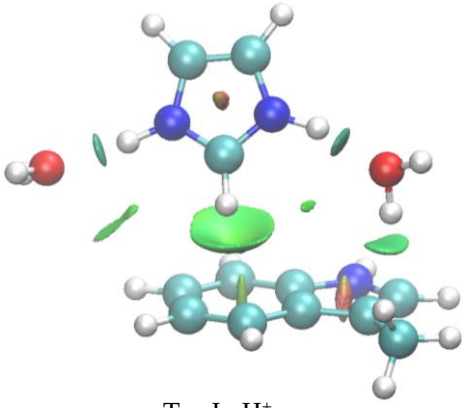


Tyr-ImH$^+$w$_1$

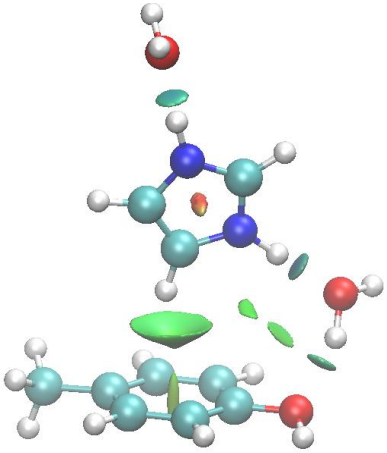
(b)



Phe-ImH$^+$w$_2$

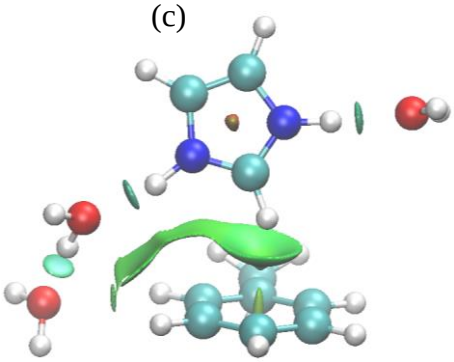


Trp-ImH$^+$w$_2$

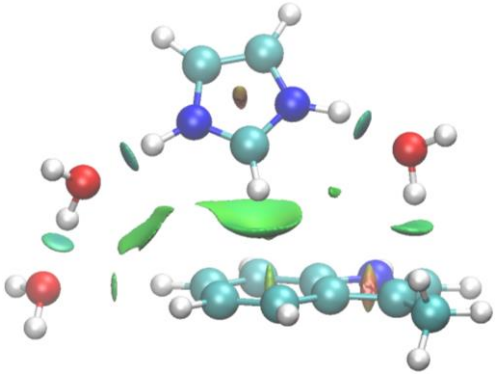


Tyr-ImH$^+$w$_2$

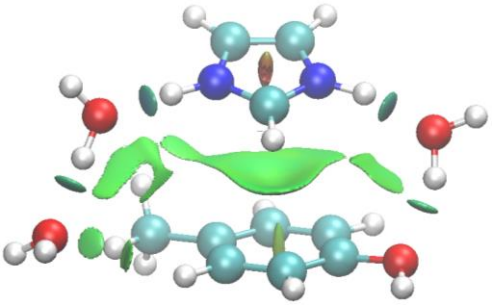
(c)



Phe-ImH$^+$w$_3$



Trp-ImH$^+$w$_3$



Tyr-ImH$^+$w$_3$

**Fig. S2** Noncovalent Index (NCI) plots of most stable geometries were obtained from DFT calculations (a) AAs-$ImH^+W_1$ (b) AAs-$ImH^+W_2$ (c) AAs-$ImH^+W_3$. The green and cyan color indicates the strong and weak interactions between the AAs and $ImH^+W_n$ clusters.

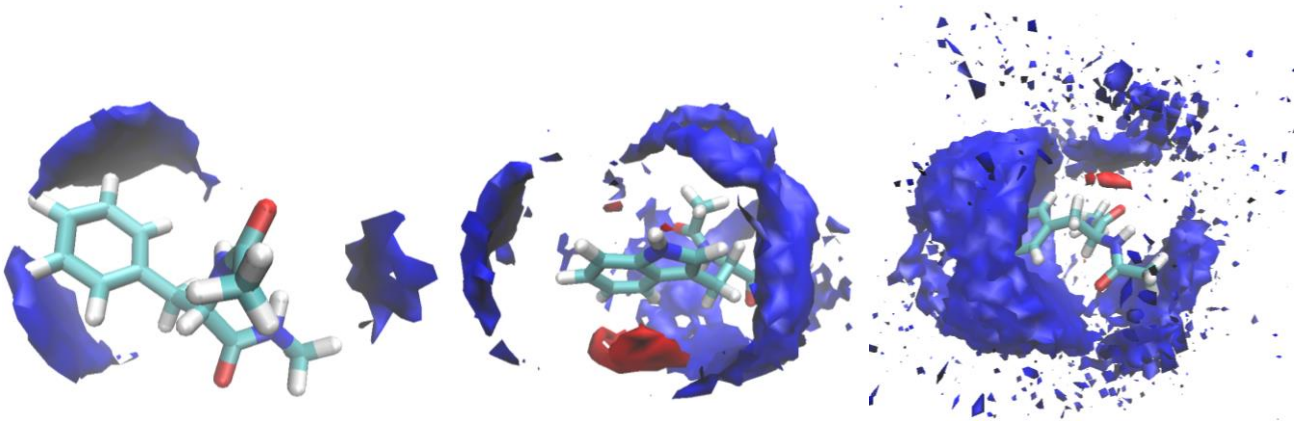



**Fig. S3** The SDF of $ImH^+$ (blue) and water (red) molecules around the AA models are shown.

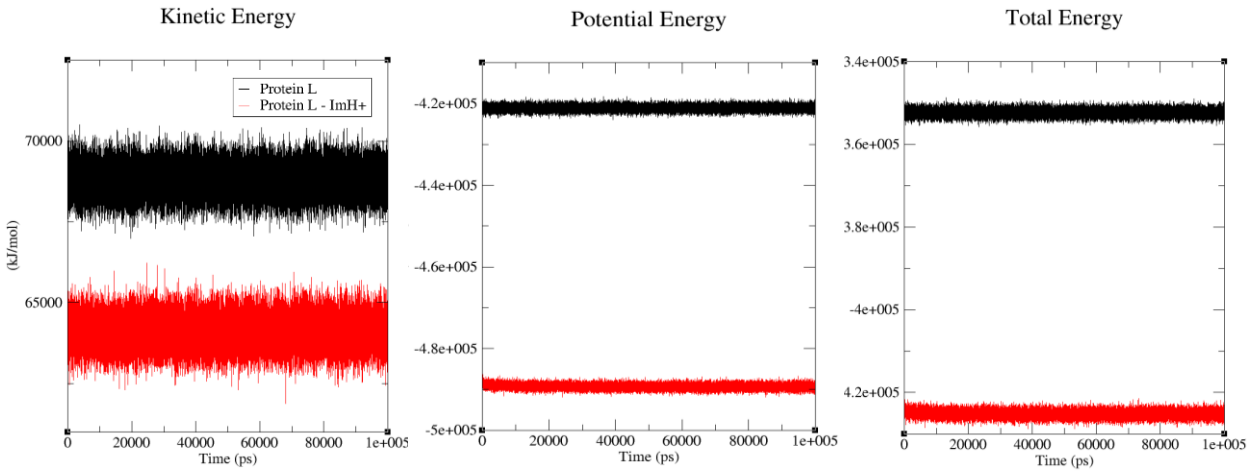



**Fig. S4** The kinetic, potential, and total energies of Protein-L and Protein-L-$ImH^+$ with corresponding to time are displayed.