Stability of non-covalent interactions involving aromatic residues in protein structures: Comparison with conventional hydrogen bonds using molecular dynamics simulations

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Abstract

Recent studies have revealed the importance of non-covalent interactions in proteins viz. conventional & non-conventional H-bonds such as C-H•••A, D-H•••A, S-H•••A [1]. Importance of interactions involving π electron cloud of aromatic residues namely C-H•••π, D-H•••π, S-H•••π, LP•••π and Cation•••π have also been recognized [2-4]. Most of these studies involved crystal structure analysis of proteins or ab-initio calculations and their interaction energy varies from -0.5 to -10 kcal/mol. It has also been speculated that such interactions could stabilize protein structures, could augment ligand-protein interactions and could be involved in enzymatic activity [1-5]. But, till date few studies have investigated the dynamic nature of such interactions and comparison of non-covalent interactions involving aromatic residues with other conventional interactions will be of great interest. Here, we report molecular dynamics simulations carried out on two different classes of globular proteins (PDB IDs: all-α - 1FAZ, 1UJ8; all-β - 1UAI). Each of the three proteins was simulated for a period of 30ns after 2 ns equilibration. We have analyzed the dynamic nature of eight different non-covalent interactions to identify how these interactions behave over time within and across the different classes of proteins. Fraction of each type of interaction that is maintained throughout the simulation, mean resident time (MRT) and the role of solvent in destabilizing the interactions are some of the analyzed properties. Our preliminary investigation reveals that conventional H-bonds are dominant (~60%) interactions and is mostly due to main-chain functional groups. They are predominantly stable with MRT at least 10 ns and this could be due to the fact that they are responsible for maintaining the secondary structures. Our analysis reveals that C-H•••A interactions involving the main-chain Cα and main-chain carbonyl oxygen are the second most dominant interactions in the all-β-protein. Large proportion of them is relatively more stable. Cation•••π interactions are less frequently observed (~2%), but surprisingly it is one of the most stable interactions. The MRT of many such interactions exceeds 20 ns. Such strong and stable cation… π interaction may be essential for the biological activity of proteins [5].

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