

Abstract Submitted
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pH-dependent Conformational Reorganization due to Ionizable Residues in a Hydrophobic Protein Interior. ANKITA SARKAR, Department of Physics, University of Florida, Gainesville, PANCHAM LAL GUPTA, ADRIAN ROITBERG, Department of Chemistry, University of Florida, Gainesville — Ionizable residues in proteins are intrinsically hydrophilic. However, ionizable residues buried in the protein interior, despite being inherently incompatible with hydrophobic environments, are responsible for major protein functions like biological energy transduction and reactions in enzymatic pathways. These buried ionizable residues display anomalous experimental pKa values. In the present work, we study the pH-dependent conformational reorganizations coupled to the ionization of lysine residues in L25K and L125K variants of staphylococcal nuclease (SNase) using constant pH replica exchange molecular dynamics simulations (pH-REMD) in explicit solvent. Our calculations show that the pKa values of lysine residues buried in the 25th and 125th positions of the L25K and L125K respectively, are significantly deviated from their pKa values in bulk water and are in good agreement with experimental values. This computational study, besides offering a detailed atomistic understanding of the structural determinants of the shifted pKa values displayed by internal ionizable residues, aids in bolstering the experimental findings.

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