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Computing the binding affinity of Zn^{2+} in human carbonic anhydrase II on the basis of all-atom molecular dynamics simulations.[1]
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Human carbonic anhydrase II (hCAII) is a metalloenzyme with a Zinc cation at its binding site. The presence of the Zinc turns the protein into an efficient enzyme which catalyzes the reversible hydration of carbon dioxide into bicarbonate anion. Available X-ray structures of the apo-hCAII and holo-hCAII show no significant differences in the overall structure of these proteins. What difference, if any, is there between the structures of the hydrated apo-hCAII and holo? How can we use computer simulation to efficiently compute the binding affinity of Zinc to hCAII? We will present a scheme developed to compute the binding affinity of Zinc cation to hCAII on the basis of all-atom molecular dynamics simulation where Zinc is represented as a point charge and the CHARMM36 force field is used for running the dynamics of the system. Our computed binding affinity of the cation to hCAII is in good agreement with experiment, within the margin of error, while a look at the dynamics of the binding site suggests that in the absence of the Zinc, there is a re-organization of the nearby histidine residues which adopt a new distinct configuration.

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