Understanding experimental properties of Cu,Zn SODs through molecular dynamics simulation - (session: Structural Genomics)

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Understanding protein hydration is a crucial, and often underestimated issue, in unravelling protein function. Molecular dynamics computer simulation has been applied to dimeric Photobacterium leiognathi Cu,Zn superoxide dismutase, comparing the water molecule sites determined using 1.0 ns molecular dynamics simulation with those detected by X-ray crystallography. 20% of the water molecules detected by the two techniques fall at common sites. Water molecules trapped in the dimeric protein inter-subunit cavity, as identified in the crystal structure, display a trajectory mainly confined within the cavity although characterized by relatively short residence times because they continuously exchange from one site to another within the cavity.
Limited proteolysis by trypsin of monomeric Cu,Zn superoxide dismutase from Escherichia coli induces a specific cleavage of the polypeptide chain at the level of Lys60 located in the S-S subloop of loop 6,5 where, if compared to the eukaryotic enzyme, a seven residues insertion, completely exposed to the solvent, is observed. Molecular dynamics simulation indicates that the S-S subloop undergoes high fluctuations and that its high flexibility coupled to an high solvent accessibility can explain the specific bond selection of the protease. As a matter of fact of the possible 14 solvent accessible proteolytic sites only the Lys60 flexible site is cleaved. These experiments suggest that molecular dynamics simulation can be used to identify proteolytic sites in proteins.