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Title: Molecular modeling of the conformational space of the knot protein DehI

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Abstract

Knot conformations in proteins are folding patterns in the amino acid chain that lead to the formation of a knot via pathways that are not yet understood. The bacteria Pseudomonas putida expresses a protein known as DehI, that serves as a halo acid dehalogenase. The tertiary conformation of DehI in the native state is a Stevedore 6-1 knot, making it one of the most complex of its kind. In the present work, we studied the influence of the charge state on the folding dynamics of the knot protein DehI. Briefly, the conformational space of DehI was sampled by coarse molecular dynamics (MD) simulations. Charge assignment was performed by scoring the accessible surface area. For example, solvent accessibility and the pKa of the acidic and basic residues were primarily used to identify and assign the charge sites. Theoretical ion-neutral collision cross section (CCS\textsubscript{N2}) was calculated for each identity vector using the TM algorithm implemented in the iMos software. A significant challenge in the folding intermediates determination is the evaluation of the large number of structures generated by MD. To overcome this problem, a clustering algorithm based on the RMSD and CCS\textsubscript{N2} of the candidates was implemented. Our results illustrate how the stabilizing molecular interactions are disrupted with the increasing coulombic repulsion, as a consequence of the charge state.