Coarse-Grained Modeling of Molecular Machines in AAA+ Family
KENJI YOSHIMOTO, CHARLES L. BROOKS III, Department of Molecular Biology, The Scripps Research Institute — We present a new coarse-grained model of the large protein complexes which belong to AAA+ (ATPase associated with diverse cellular activities) family. The AAA+ proteins are highly efficient molecular machines driven by the ATP (adenosine triphosphate) binding and hydrolysis and are involved in various cellular events. While a number of groups are developing various coarse-grained models for different AAA+ proteins, the molecular details of ATP binding and hydrolysis are often neglected. In this study, we provide a robust approach to coarse-graining both the AAA+ protein and the ATP (or ADP) molecules. By imposing the distance restraints between the phosphates of the ATP and the neighboring $C_{\alpha}$ of the proteins, which are used to conserve a typical motif of ATP binding pocket, we are able to predict large conformational changes of the AAA+ proteins, such as replicative hexameric helicases. In the case of the hexameric LTAg (large tumor antigen), the backbone RMSD between the predicted ATP-bound structure and the X-ray structure is 1.2 Å, and the RMSD between the predicted ADP-bound structure and the X-ray structure is 1.5 Å. Using the same approach, we also investigate conformational changes in the hexameric E1 protein, whose X-ray structure was recently solved with ssDNA, and give some insights into the molecular mechanisms of DNA translocation.

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