Abstract

In this study we analyzed proteins that are structured and unstructured. A new algorithm named *Layers* is introduced with a novel protein structure transformation feature named Residue Transition Pattern (RTP). *Layers* performs molecular surface extraction, deterministic surface sampling at tunable fineness besides RTP generation. Sampling with *Layers* is shown to preserve global protrusions of molecular surface. Whereas, RTP is robust in identifying similarities between proteins which could be challenging for conventional sequence or structure comparison methods. *Layers* is used to analyze 7,624 single polypeptide chains and 16,983 domains and is available at http://www.csb.iitkgp.ernet.in/applications/mol_layers/main. We have also adopted *Layers* to study antigen-antibody complexes and proposed a concept of anchored residues in terms of *Layers,* which is shown to have a positive propensity of 0.49 in B-cell epitope. An optimum sampling cutoff for *Layers* is also proposed which preserves 50% of epitope while retaining only one-third of a molecule. Combination of anchor residues with other parameters were used to develop a prediction model with 89% epitope prediction accuracy. Besides analyzing the static structures of proteins, we also used Molecular Dynamics (MD) simulations to study the polymorphic conformations of intrinsically disordered proteins. Deleted in split hand/split foot protein 1 (DSS1) is used as a model protein and is studied in 12 different configurations. These configurations include combinations of mutations, two different water models, bound and unbound states of DSS1 to BRCA2. We have identified that the secondary structure in bound DSS1 is transient besides being tolerant to mutations as a consequence of its flexibility as it remains bound to BRCA2. Effect of mutations on conformational dynamics of DSS1 were studied and also established that Tip4P is a suitable water model for studying the dynamics of DSS1. Our findings provide a framework for understanding the dynamics of DSS1-BRCA2 interactions.