Computer-aided modelling of protein conformations and ligand binding

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Abstract

Processes like ligand binding, chemical modifications or changes in environmental conditions may result in conformational switching in proteins, affecting their function. The loss of associated function may also result in disease causing pathological conditions. Computer-aided modelling and simulations of protein systems serve as an important tool to study protein dynamics. By employing certain proteins and peptide models we have tried to understand two aspects of protein dynamics: folding and ligand binding. For folding, we modelled systems involved in local conformational changes such as Alzheimer's causing α→β transitions and sequences involved in early events of protein folding. Characterization of these model systems, with or without the protein context, revealed the importance of primary sequence, environmental conditions, and tertiary contacts provided by the pre-existing protein environment. In ligand binding studies, blind docking simulations and structure-based screening methods were used. Investigation of structural features and specific protein-ligand interactions determined binding pose and hence distinguished binders from non-binders. These features may be used to design scoring functions for developing accelerated screening methods and drug designing.

Keywords Protein Folding, Conformational Modelling, Ligand Binding, Molecular Dynamics, Molecular Docking