Poster

Method of extending rotamer libraries and its usage in protein active site studies

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Protein rotamer libraries are extensively used during the protein modelling process and have been shown to greatly improve the prediction of protein-ligand and protein-protein interactions as well as suggest amino acid mutations. Most of the strategies predicting the side-chain conformations involve calculating the dihedral angle averages for each side-chain from a subset of high-quality protein structures. However, these methods, while fast to apply, tend to average out rarely observed dihedral angles [1] and ignore the surrounding atoms. In order to create a well-rounded rotamer library, we have developed a method [2] to generate rotamer libraries from a single structure without the need to process large subsets of side-chain occurrences.

The method utilizes a force-field to incorporate interactions with surrounding atoms and can detect rare dihedral angle occurrences. Due to the method's flexibility, we opted to incorporate heteroatoms, thereby opening up a possibility to store and generate heteroatom positions in the same format as the rotamer libraries. Initially, metal ions and water molecules were analysed. The research focused on type II restriction endonuclease active sites to demonstrate the utility of the extended rotamer libraries by determining the quantity of metal ions in the active site – a currently unsolved problem [3].

In the future, the method could incorporate more complex ligand data. By utilizing chemical structure data from the Crystallography Open Database [4], it could suggest potential ligands for the desired target proteins.

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