

## The *rotag* library: generating protein structure-specific side-chain rotamer libraries

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Identifying the probable positions of the protein side-chains is one of the protein modelling steps that can greatly improve the prediction of protein-ligand, protein-protein interactions. With some exceptions, most of the strategies predicting the side-chain conformations use predetermined angles, also called rotamer libraries, that are usually generated from the subset of high-quality protein structures. Although, these libraries are very useful when selecting possible side-chain atom positions, the overall validity and usability regarding specific protein structure should be studied further.

In order to get well-rounded rotamer library, there should be the balance between the coverage and the quantity of possible side-chain positions. The lack of possible side-chain rotamers will hinder the correct selection of atom positions and the over abundance – the fast selection for protein structure predictions.

We are suggesting the approach that would cover both the coverage and the accuracy of the rotamer library. The *rotag* software was developed in order to accommodate both these problems. It scans side-chain conformations using dead-end elimination strategy and evaluating potential energies on each calculation step.

The additional challenge that we faced was to have proper method to compare rotamer libraries. The best-case RMSD, best-case dihedral angles and average rotamer choice parameters were selected as good candidates for the comparisons. Multiple rotamer libraries were compared: Dunbrack, Dynameomics, Penultimate and those generated with *rotag*.

The comparisons revealed that the rotamer libraries that were created from the subset of existing protein structures sometimes lack rotamer positions for certain side-chains of the target proteins. Using more flexible methods, such as *rotag*, increases the probability of the inclusion of correct conformations. However, not in all cases these flexible methods produce the correct subset of potential candidates.

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