

MS10-P5 Detection of *trans* – *cis* flips and peptide plane flips in protein structuresWouter G. Touw¹, Robbie P. Joosten², Gert Vriend¹

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Peptide bonds connect adjacent amino acids in proteins. The partial double bond character of the peptide bond restricts its torsion and the dihedral angle ω ($C\alpha_{i-1} - C_{i-1} - N_i - C\alpha_i$) only has values around 180° (*trans*) or 0° (*cis*). Many *cis* peptide bonds have been incorrectly modelled in the PDB (Protein Data Bank) as *trans* peptides or *vice versa*. A coordinate-based Random Forest classifier is presented to detect peptide bonds that need either a *trans* – *cis* flip or a 180° flip of the entire peptide plane. Like the method developed by Weiss & Hilgenfeld (1999), the prediction is based on the distorted local geometry of the local protein backbone when it is forced to adopt an incorrect conformation. The prediction performance on 1088 independent manually validated test cases was excellent for all flip types and for all amino acid types. The method predicts thousands of corrections in the PDB. Several examples were found in which the necessary flip causes our understanding of the structure function relation of the molecule to radically change.

Keywords: peptide flip, *cis* peptide bond, structure validation**MS10-P6** Novel network perspective on the structure, function and dynamics of proteinsMario Albrecht¹, Doncheva T. Nadezhda²

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In recent years, a new interdisciplinary area of research that combines network science and structural biology in the context of visual analytics has emerged. By representing protein structures as networks of interacting residues and applying network visualization and analysis techniques, we facilitate the analysis of structure-function relationships and gaining more insight into complex molecular mechanisms such as protein-protein and protein-ligand interactions. To this end, we offer a software suite (including our tools RINalyzer and RINerator) that supports interactive, multi-layered visual analysis of protein structures and their molecular function in protein binding, allostery, drug resistance and other interaction mechanisms. In particular, our integrative approach can be applied to visually analyze the impact of sequence mutations on protein structure.

To capture the dynamic nature of protein structures and interactions, we also developed a special approach to visualizing and analyzing ensembles of protein structures as generated by MD simulations or NMR. We use dynamic, weighted residue interaction networks (dRINs) that account for the different protein conformations within the ensemble. Possible applications of this approach include the identification of structurally and functionally important residue interactions, the comparison of ligand-binding modes in protein interactions, as well as the characterization of protein mutations and their effect on structure and function (see Figure).

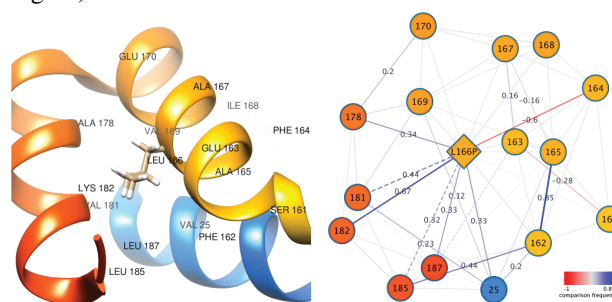


Figure 1. Close-up on the mutation L166P in the DJ-1 wild-type structure with PDB identifier 1PDV (left) and in the comparison dRIN (right). Network edges correspond to non-covalent residue interactions that are more frequent in the wild-type (blue lines) or mutant (red lines) structures.

Keywords: protein structure, protein function, residue network, molecular dynamics, NMR, visual analytics