

# Interactive online toolbox for sequence-structure-function analysis based on comprehensive mutation data

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The collection of genetic variations in proteins, their comparison and molecular analysis of the three-dimensional structures of proteins are important for the identification and interpretation of biologically relevant residues to explain gain or loss of function mutations which may cause diseases. Databases to collate functional data of experimental studies have been published, but tools to analyze the molecular effects of mutations in combination with structural data are as yet poorly provided.

Here, we present our Sequence-Structure-Function-Analysis toolbox which offers search and visualization tools for studying structural and functional properties of individual amino acid residues either by two-dimensional features such as interactive and user-defined snake-plots or by three-dimensional structures. The interactive mapping of functional information onto the three-dimensional structures allows elucidation of crucial residues for intra- or intermolecular interactions thus providing deeper insights into molecular activation mechanisms.

The interpretation of functional findings is supported by receptor morphings simulating intramolecular changes during the activation process, which thus help to trace the potential function of each amino acid and provide clues about the local structural environment, including potentially relocated spatial counterpart residues. The functional data are converted into relational percentage values, thereby the system allows the comparison and classification of data from different proteins and various experimental approaches. Our toolbox has been incorporated into a freely available database and website for the Glycoprotein Hormone Receptors (<http://www.ssfa-gphr.de>), but the framework may also be adaptable to other macromolecules.