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Selection of the most significant ligand-receptor interactions in GPCRs crystal complexes

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G Protein-Coupled Receptors (GPCRs) comprise a large superfamily of signalling proteins (800 receptors), which are involved in a number of physiological processes, like mood and behaviour regulation, perception of pain, autonomic nervous system transmission, inflammation, regulation of immune system, etc. [1]. Despite the fact that up to 59 receptors have been drugged, only 159 crystal structures are available in PDB in total (for 35 targets).

These structures were utilized in the new pharmacophore method [2] based on the library of interacting ligand moiety-residue pairs extracted from the crystal structures. Here we automate the methodology using interaction fingerprints for the systematic analysis of the growing number of crystal structures and the extraction of fragments. In addition we extend it to the homology models, investigating the effect of conformational flexibility in the quality of the pharmacophore models.

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References

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