MOLECULAR MODELLING OF SEROTONIN 5-HT_{1A} RECEPTOR USING AUTOMATED DOCKING OF BIOACTIVE COMPOUNDS WITH DEFINED GEOMETRY. NOVEL APPROACH TO GPCR MODELLING

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Molecular model of serotonin 5-HT_{1A} receptor was constructed by homology modelling (MODELLER 7v7) on the template of bovine rhodopsin X-ray structure. 400 conformations of the receptor were produced and evaluated by automated docking (FlexX) of bioactive, conformationally constrained arylpiperazine derivatives. Such inverse virtual screening was based primarly on the occurance of interactions between ligand and most important aminoacids (especially $Asp^{3.32}$) and the interaction energies scored by different scoring functions with concensus scoring (CScore) algorithm. The first step results showed the crucial role of $Asp^{3.32}$ conformation, the most probable binding site and ligand binding mode. The best models were used for docking of wide group of arylpiperazines with different structure and conformational flexibility. Ligand conformation, binding mode and possible interactions with binding site residues were observed and discussed with reference to previous studies in this field.