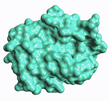
RECEPTOR·AI

AI-POWERED WORKFLOW TO GENERATE ENSEMBLE OF PROTEIN CONFORMATIONS FOR VIRTUAL SCREENING

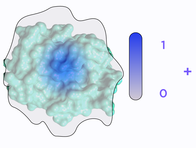
Determination of the most relevant binding pockets starts from the target protein structure and follows two parallel routes:

TARGET PROTEIN



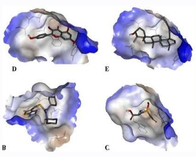
1. An AI model of pocket prediction is used, which assigns the scores to each residue reflecting its probability to be part of the binding pocket based on the knowledge inferred from the set of all known protein-ligand complexes. After that, the probability map is post-processed, and the tentative binding pockets are determined. They are compared to complemented by available literature data by means of AI-based mining.

AI POCKET PREDICTION



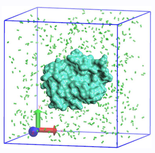
LITERATURE MINING (LLM) + EXPERIMENTAL DATA

PROSPECTIVE POCKETS

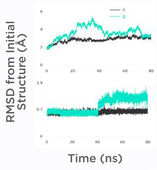


2. MD simulations of the target protein in its native environment, which generates equilibrated MD trajectories. The trajectories are processed and aligned and are subject to clustering by our proprietary software. The cluster centres represent the typical structures of the distinct regions of the sampled conformational state, including rare and transient structures.

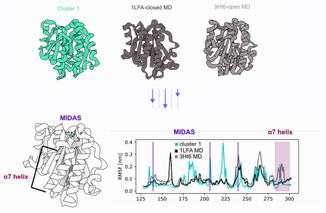
MD SIMULATION



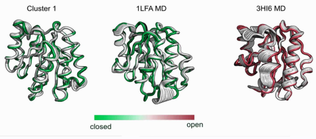
MD TRAJECTORIES



CLUSTERING



REPRESENTATIVE CONFIRMATIONS

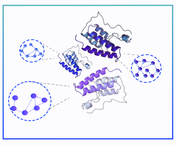


Both routes converge to the ensemble of protein conformations, which are used for subsequent virtual screening.

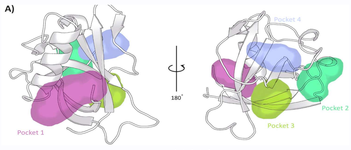
We utilise the stock chemical space and perform the initial screening against a selected subset of the most distinct protein conformations. The shortlisted compounds are subject to secondary screening, which involves molecular docking with AI rescoring using the whole ensemble of conformations. The final hit candidates are attributed to the binding pockets and particular protein conformations, annotated and forwarded to experimental validation of affinity and/or activity.

The confirmed hit compounds are used to determine the most promising binding pocket position and conformation for subsequent stages of production virtual screening.

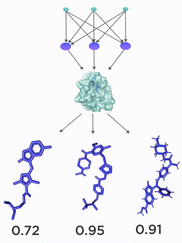
STOCK CHEMICAL SPACE

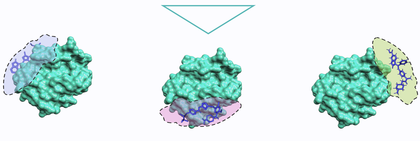


ENSEMBLE AI-BASED VIRTUAL SCREENING TO PROSPECTIVE BINDING POCKETS



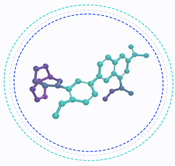
AI DOCKING





ATTRIBUTING LIGANDS TO POCKETS

SELECTION OF MOST PROMISING POCKET



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