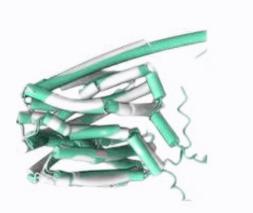
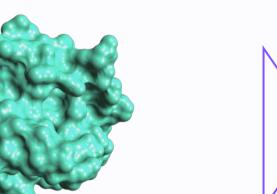


Novel structure-based selectivity worlflow based on the ensemble of differential pharmacophore representation, which allows leveraging the structural and dynamic differences between highly similar proteins.





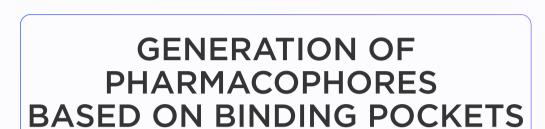


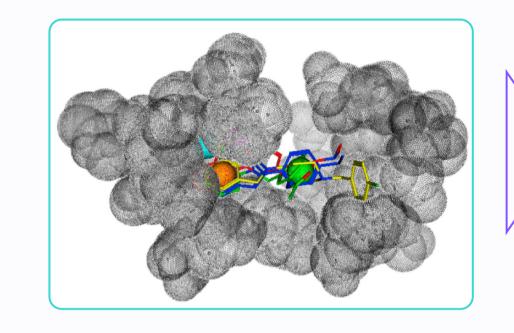
TARGET PROTEIN

OFF-TARGETS



GENERATION OF PROTEIN CONFORMATIONS





For each conformation of the target

binding pocket is generated. These

and off-target proteins, the pharmacophore model of the

models are then superimposed,

algorithm, which emphasises the

pharmacophore bits that are unique and specific to the target protein.

dynamical distinctive features of the

binding pocket in the target protein.

aligned and analysed by our

proprietary feature detection

The resulting model is called a

represents both structural and

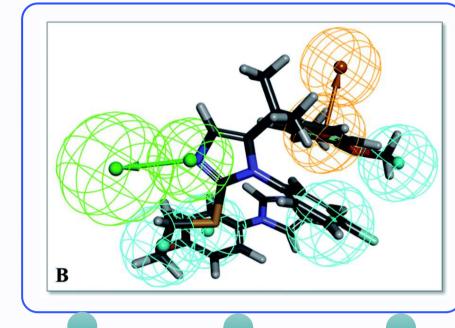
differential pharmacophore and



GENERATION OF PROTEIN OF CONFORMATIONS

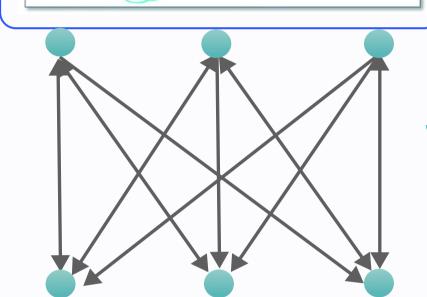
The target and all off-targets are subject to all-atom MD simulations in their native environment. The MD trajectories are processed by the proprietary clustering algorithm, which extracts the sets of representative protein conformations which account for overall protein flexibility and the local dynamics of the binding pocket of interest. For each protein, the ensemble of the most relevant conformations is formed.

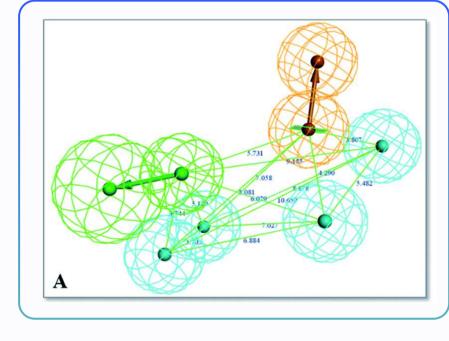




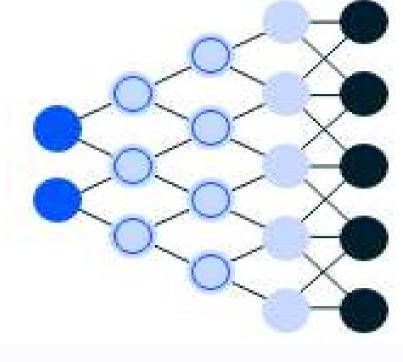
SELECTION OF SPECIFIC

PHARMACOPHORES



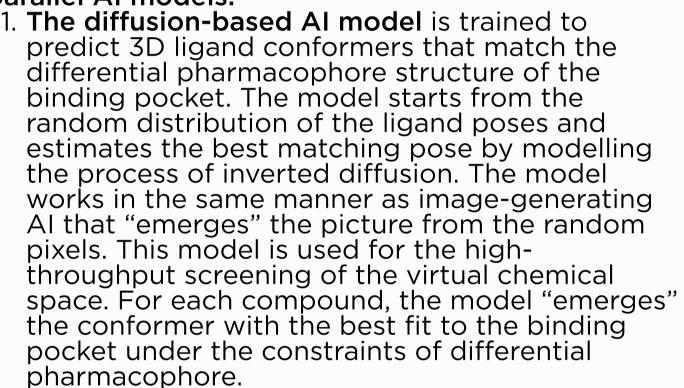


OFF-TARGET PHARMACOPHORES

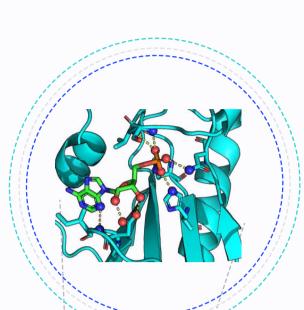


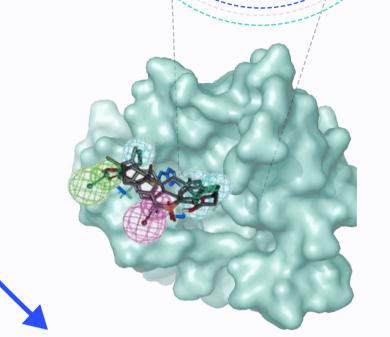
GENERATIVE AI: PHARMACOPHORE -> BINDING POSE

The differential pharmacophore is then used in two parallel AI models:



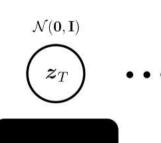
2. The generative model follows the same logic, but instead of screening the pre-defined chemical space, it generates the compounds on the fly by means of a molecular transformer neural network. The compound is generated in the 3D pose that fits the best to the differential pharmacophore.

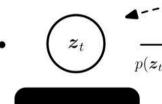


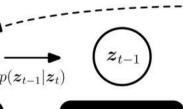


PREDICTED POTENT AND
SELECTIVE COMPOUNDS FOR
TARGETS BASED ON SET OF
CUSTOM AI SCORING
FUNCTIONS TO SELECT THE
BEST BINDING POSE

DIFFUSION-BASED SCREENING MODEL (POCKET PHARMACOPHORE -> BINDING POSE)

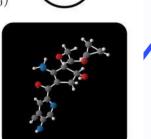


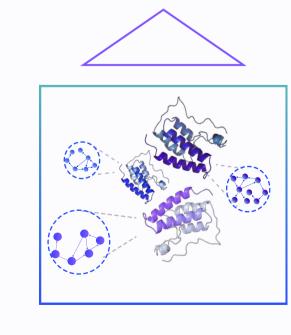












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