# HYDE - Scoring

BioSolveIT
expect actives!

Understand binding and where to improve. HYDE gives you visual and intuitive binding affinities and acts as an eye-opener to plan the next step in your drug-design process.

How does HYDE work?

Your lead compound is not perfectly binding yet and you would like to know why. The core of this very task is "scoring", i.e., the affinity assessment of a ligand in a binding pocket. HYDE is our method to address the prediction of ligand binding affinity. It calculates realistic Free Energies of binding and pinpoints affinity problems if a bound ligand. The visually processed information allows interactive hypothesis generation and validation to reason about the best possible next step.
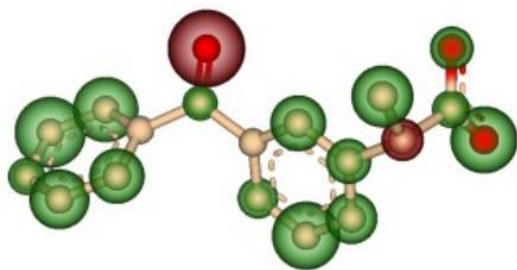
HYDE is patent protected and worldwide unique as it is not trained, calibrated, or fit on any particular data. Affinity predictions are generally possible for protein-ligand complexes, protein-protein interactions, as well as DNA & RNA binders. It is based on physical principles only by linking the two major driving forces, desolvation and interactions, in a sound scientific manner. HYDE is constantly improved and originated from a collaboration with BAYER, Hamburg University, and BioSolveIT.

Advantages

- Interactive and iterative optimization of leads
- Compound classification: binders/weak binders/non binders
- Innovative approach compared to trained scoring functions
- Interpretable, visual feedback
- Implicit Hydrogen bonds and DEhydration

Interactive, desolvation-aware visual ΔG estimates

The values are estimated based on a difference calculation between the bound and unbound state, based on an atomic logP-based mathematical kernel. The system has NOT been trained to specific targets, instead H-bond contribution and dehydration ("desolvation") are intrinsically balanced without weighting parameters as seen in all other force fields. By design, HYDE allows the visualization of ΔG on atoms so that the user instantly gets a feedback on the computational details behind.

HYDE will explain what can be improved here; some of these scenarios could be:

- Desolvation penalties for buried hydrophilic atoms
- Weak/questionable H-bonds
- Indifferent scaffold or linker, not contributing to ΔG
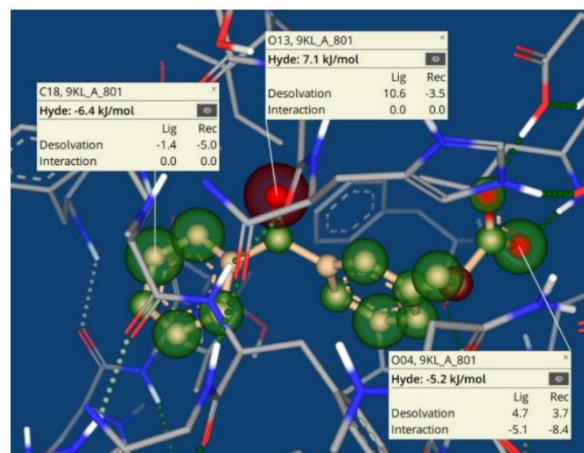
The beauty is: The moment you see it, it becomes obvious. HYDE will present you the data in an unbiased way. Now leverage from your expertise; you know best what and how to make of it. Interactively probing your complex is now possible: Exchange an unfavorable donor by a hydrophobic function or even an acceptor. Smallen the compound to improve the ligand efficiency. Find the best possible substitution pattern – all fast and under full visual control.

Mass export of protein structures

Running HYDE in the command line allows users to export huge amounts of target-ligand complexes as pdb files. This comes in handy to generate huge amounts of data for machine learning or AI approaches to train your system.

Literature

Reulecke, I.; Lange, G.; Albrecht, J.; Klein, R.; Rarey, M. Towards an Integrated Description of Hydrogen Bonding and Dehydration: Decreasing False Positives in Virtual Screening with the HYDE Scoring Function. *ChemMedChem* **2008**, *3* (6), 885–897.
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https://doi.org/10.1007/s10822-012-9626-2