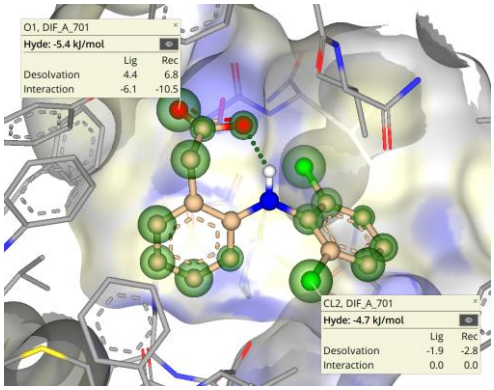
HYDE – Scoring

BioSolveIT
expect actives!

Understand the binding mode 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 pin-points 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 receives a feedback on the computational details behind.

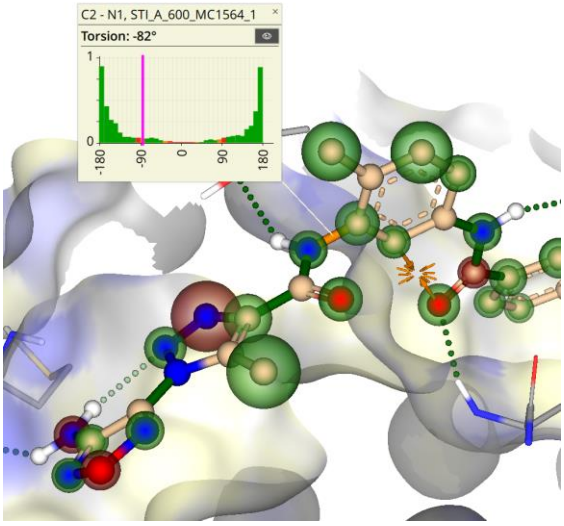
HYDE will explain what can be improved. Some of these scenarios could be:

- Desolvation penalties for buried hydrophilic atoms
- Weak or questionable hydrogen 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. Decrease the size the compound to improve the ligand efficiency. Find the best possible substitution pattern – all fast and under full visual control.

Holistic assessment of your complex

Additionally to the affinity calculations, HYDE checks for potential inter- and intramolecular clashes of your target-ligand complex and assesses the quality of the molecule's torsions.



Those can be invaluable allies to filter for the best poses of your ligands. Again, those parameters can show you potential areas for improvement.

Literature

Schneider, N.; Lange, G.; Hindle, S.; Klein, R.; Rarey, M. A Consistent Description of HYdrogen Bond and DEhydration Energies in Protein-Ligand Complexes: Methods behind the HYDE Scoring Function. *J. Comput. Aided. Mol. Des.* **2013**, *27* (1), 15–29.
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