

How well does docking work? How can it get better?

- How well does it work?
 - Fairly successful at generating binding poses [Damm-Ganamet et al, 2013]. Usually successful (~80%) at ranking them.
 - Poorly correlated with binding free energies [Warren et al, 2006].
 - Unreliable at separating actives from decoys [Cross et al, 2009].
 - Sometimes successful at virtual screening. Hit rates < 20%.
- How can it be better?
 - Free energy includes both enthalpy and entropy. Docking scores usually exclude entropy.
 - Water often mediates protein-ligand interactions. Docking usually does not consider it.
 - Polarizability. Ligands can adapt to the protein environment. Docking usually does not consider this.

References

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