

Phyre2.2: A web server to predict protein structure and protein/ligand complexes

Phyre2.2

Harold R Powell, Eleanor Stevens, Anja Conev, Suhail A Islam,
Alessia David & Michael J E Sternberg +

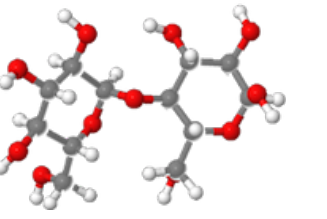
Department of Life Sciences, Imperial College London, London SW7 2AZ, UK

m.sternberg@imperial.ac.uk <https://www.sbg.bio.ic.ac.uk/phyre2/>

See Powell et al *Journal of Molecular Biology* (2025): 168960. (source of figures)

Phyre2.2

Ligand



Phyre2.2 is the next generation of the popular Phyre2 protein structure prediction portal that enables a user to find the closest AlphaFold2 model which is then used as the template.

We introduce LigandFinder and Phyre2.2-Ligand which allow for template-based ligand inheritance and prediction of protein/ligand complexes.

Phyre2.2: AlphaThread and Normal Modes

- Phyre continues to be widely used with ~40,000 unique users and 900 citations in 2024 due to its ease of use, analysis features and batch processing.
- Template-based modelling provides a complementary approach to AlphaFold.
- Phyre2.2 is the next generation of Phyre2:
 - in “AlphaThread mode” it finds the closest AlphaFold model to use as the template.
 - in “normal mode” searches an extended template library including apo- and holo-structures if available.

LigandFinder and Phyre2.2-Ligand

- Phyre2 models were long used by the community for docking ligands in drug discovery tasks
- Experience of homology modelling within Phyre2 can naturally be extended to identifying ligand transplants and complemented with docking
- LigandFinder finds ligand-bound homologues, then directs to Phyre 1-1 threading and ligand inheritance
- Phyre2.2-Ligand allows users to seamlessly:
 - inherit ligands from templates
 - dock ligands with AutoDock Vina

Phyre2.2 – Algorithm

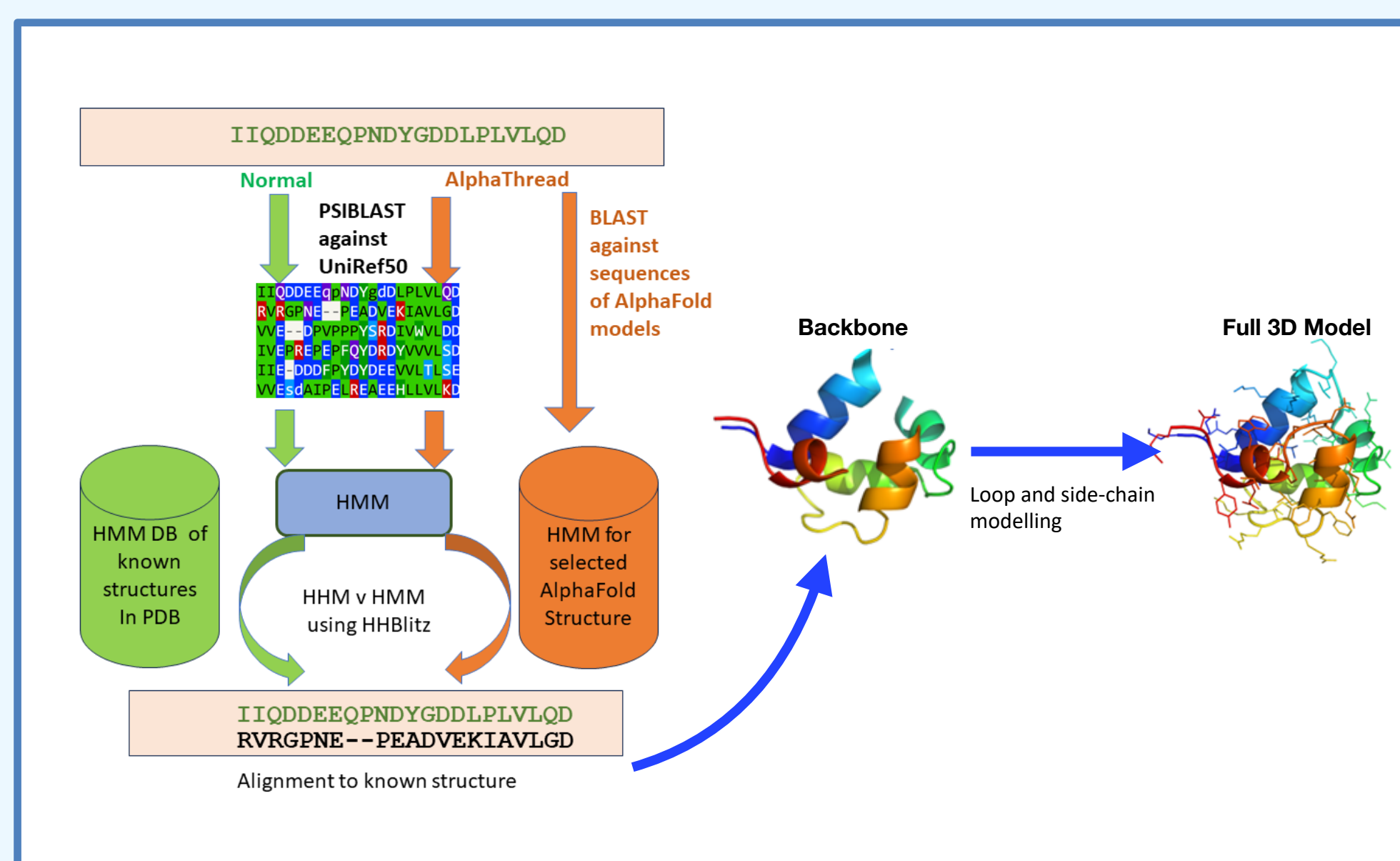


Figure 1: Flow chart of Phyre2.2 in normal (green) and AlphaThread (orange) modes.

LigandFinder – Algorithm

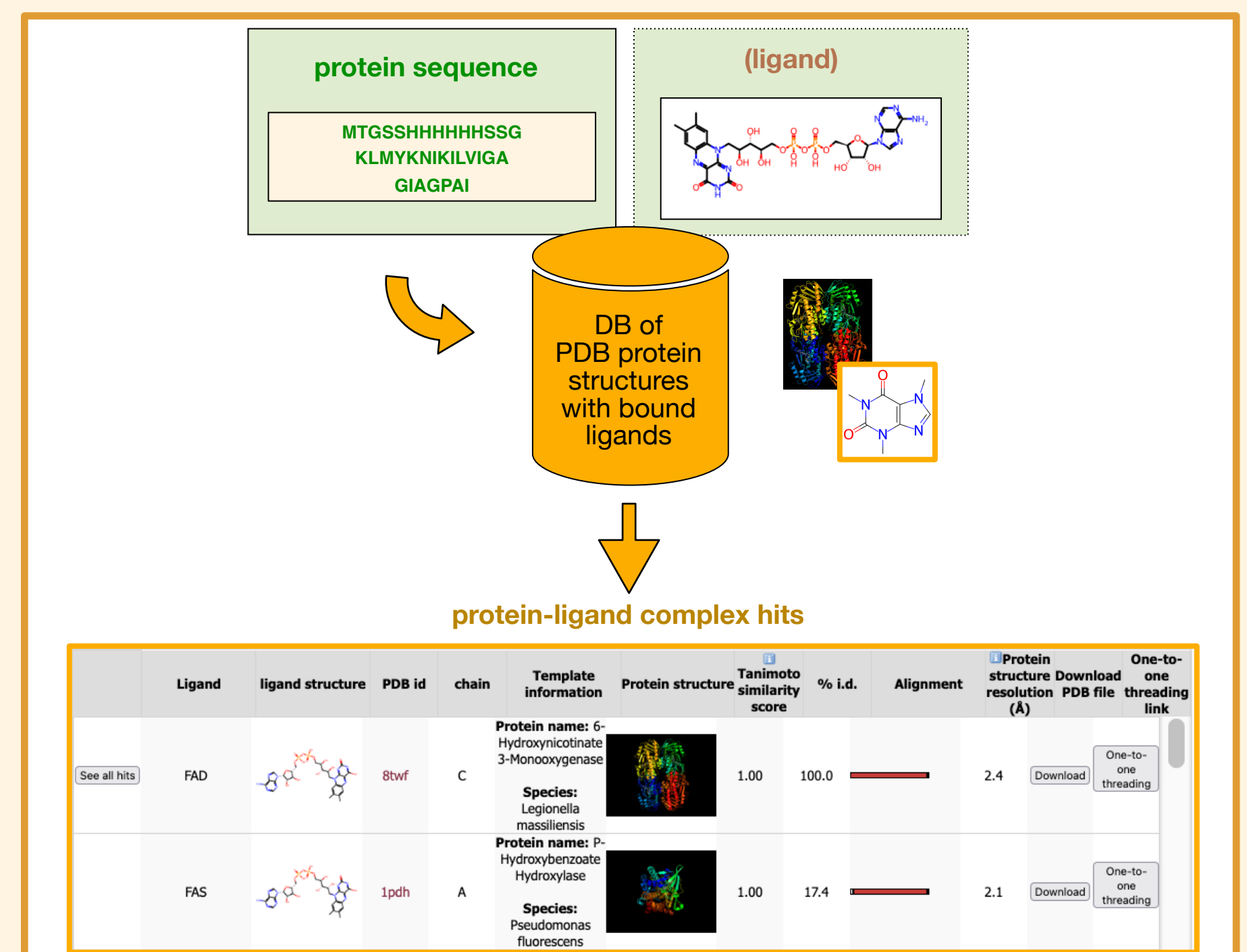


Figure 2: Flow chart of LigandFinder.

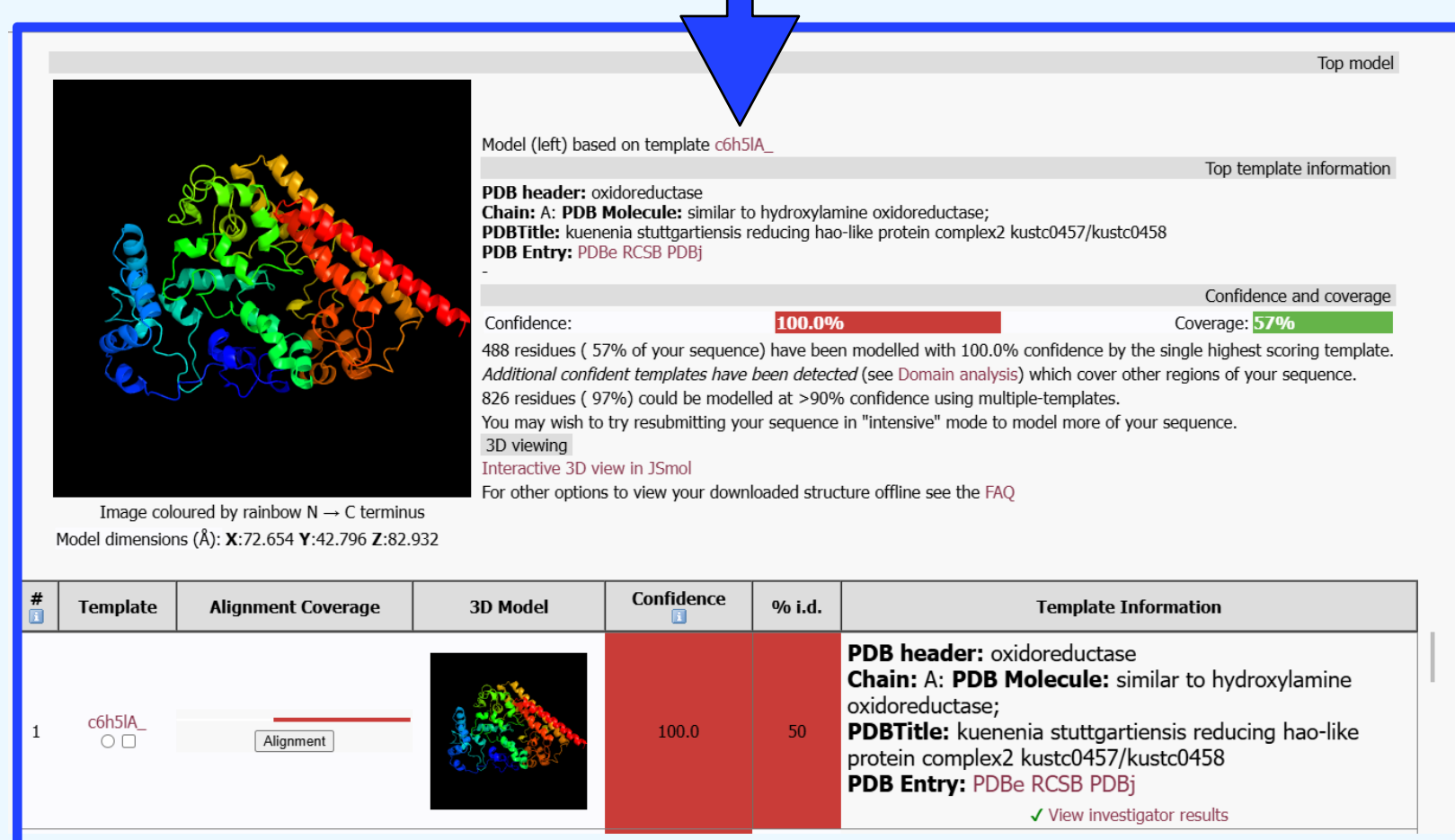


Figure 3: Output page of Phyre2.2.

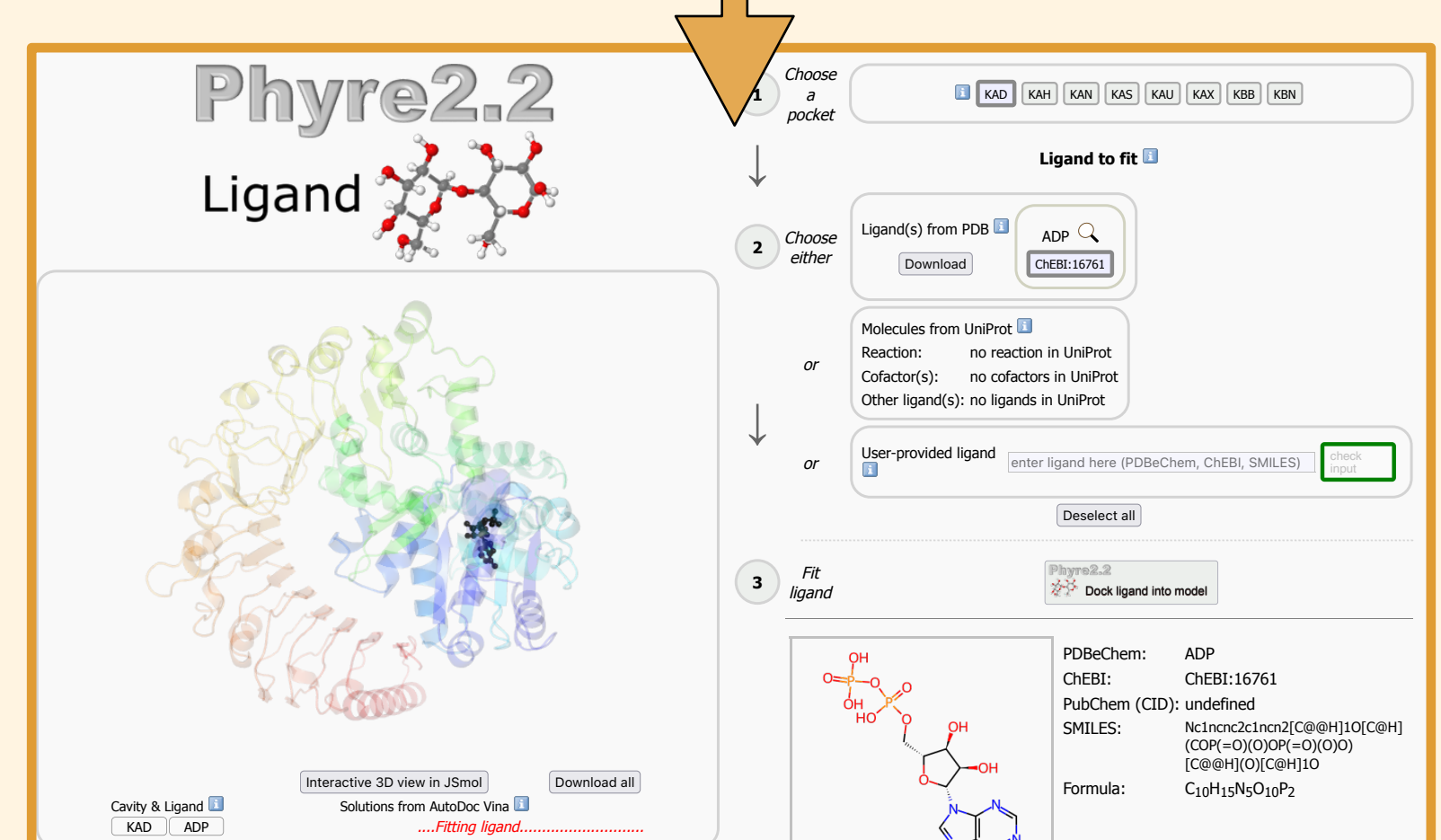


Figure 4: Output page of Phyre2.2-Ligand.