The first OpenBind release: An open experimental structure–affinity dataset and benchmark for structure-based AI

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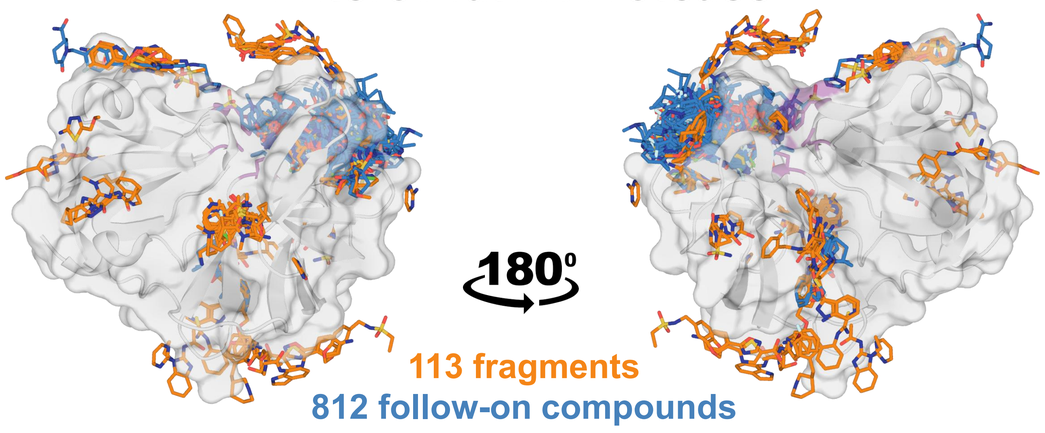
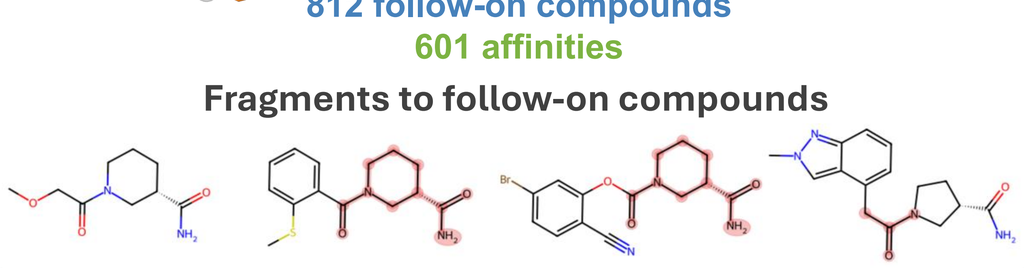
1. A coherent experimental structure–affinity dataset

Enteroviral 2A Protease



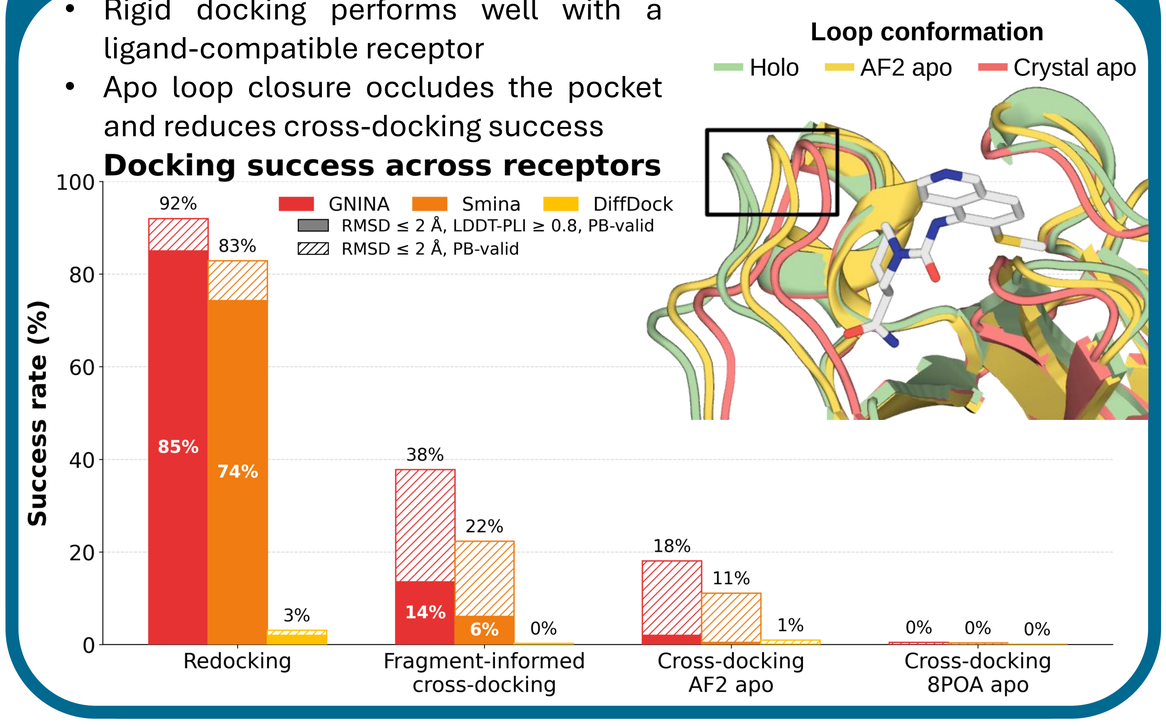
113 fragments
812 follow-on compounds
601 affinities

Fragments to follow-on compounds

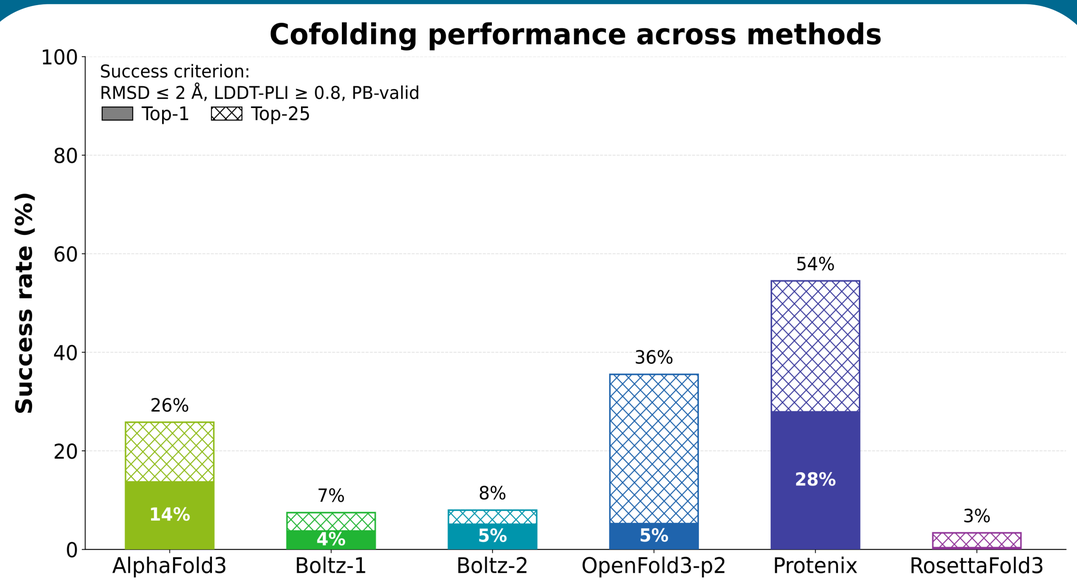


2. Receptor state influences docking performance

- Rigid docking performs well with a ligand-compatible receptor
- Apo loop closure occludes the pocket and reduces cross-docking success

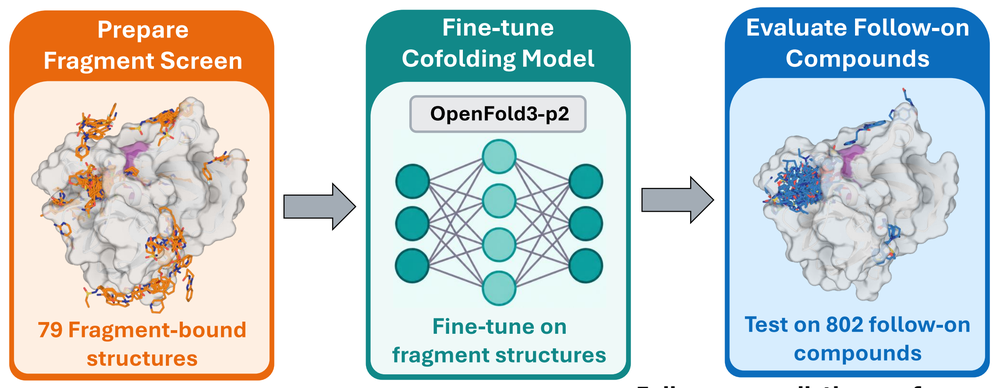


3. Pose recovery and ranking limit cofolding performance

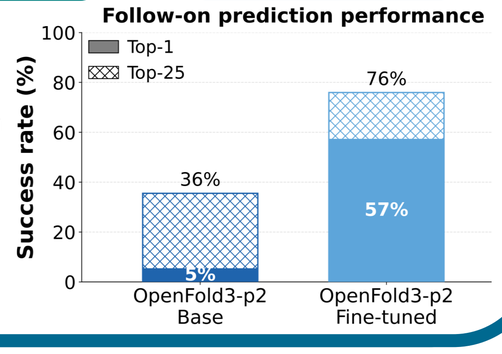


- Performance varies substantially across current cofolding methods
- Top-25 success rate remains limited, with pose ranking further constraining performance

4. Learning from fragment-bound structures



- 79 curated fragment-bound structures were used for target-specific fine-tuning
- Fine-tuning increased Top-1 success from 5% to 57% on 802 curated follow-on complexes
- For this dataset, experimental fragment data provided a strong target-specific signal for follow-on pose prediction



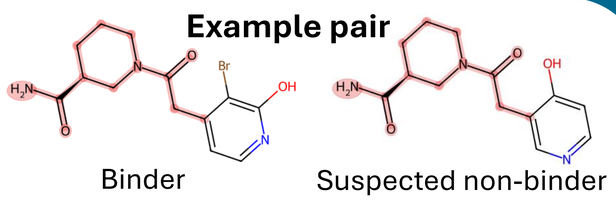
5. Virtual screening among related follow-on compounds

Benchmark composition

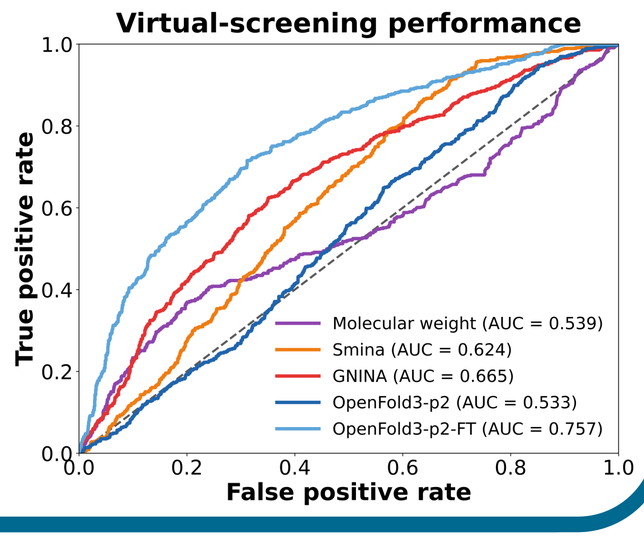
2,084 compounds

566 binders | **1,518 suspected non-binders**

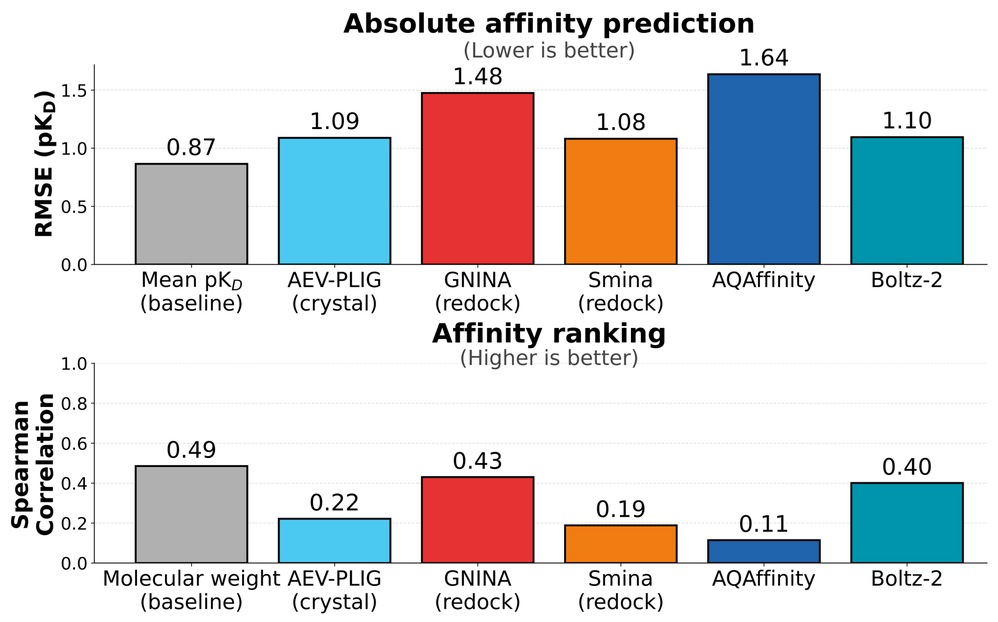
Example pair



- Suspected non-binders showed no crystallographic binding despite a successful soak
- Many binders have close analogues among suspected non-binders
- Fine-tuning increased OpenFold3-p2 ROC-AUC from 0.533 to 0.757, moving it from worst to best performer



6. Structure-based affinity prediction is challenging



- Absolute affinity prediction and ranking are weak across tested methods
- Simple baselines outperform the evaluated structure-based methods

7. Summary and conclusions

- OpenBind releases a coherent experimental structure–affinity dataset
- Docking performance depends strongly on receptor state, while cofolding remains limited by sampling and ranking
- Fragment-informed fine-tuning can substantially improve both follow-on pose prediction and virtual-screening performance
- Current methods struggle to translate structure into quantitative affinity, with simple baselines still competitive

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OpenBind
www.openbind.uk

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