

# Systematic evaluation of computational tools to identify potential drug-resistant mutations in the absence of experimental complexes

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## Can we use Al programs to model biological molecules to study mutations and their potential effect on drug resistance?

• **Drug resistance** caused by **mutations**, especially in many rapidly-evolved systems such as viruses, bacteria, and human cancer cells, raises significant global health concerns.

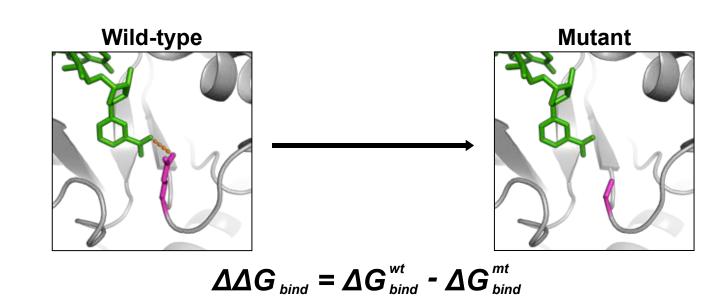


Fig 1. Effect of mutations on drug binding

- •While many researchers incorporate **Artificial Intelligence** (AI) programs like **AlphaFold2** to study mutations and drug resistance, there is no systematic assessment on the methods to identify potential drug resistant mutations without using experimental structures.
- · Here, we presented this work to fill the gap.

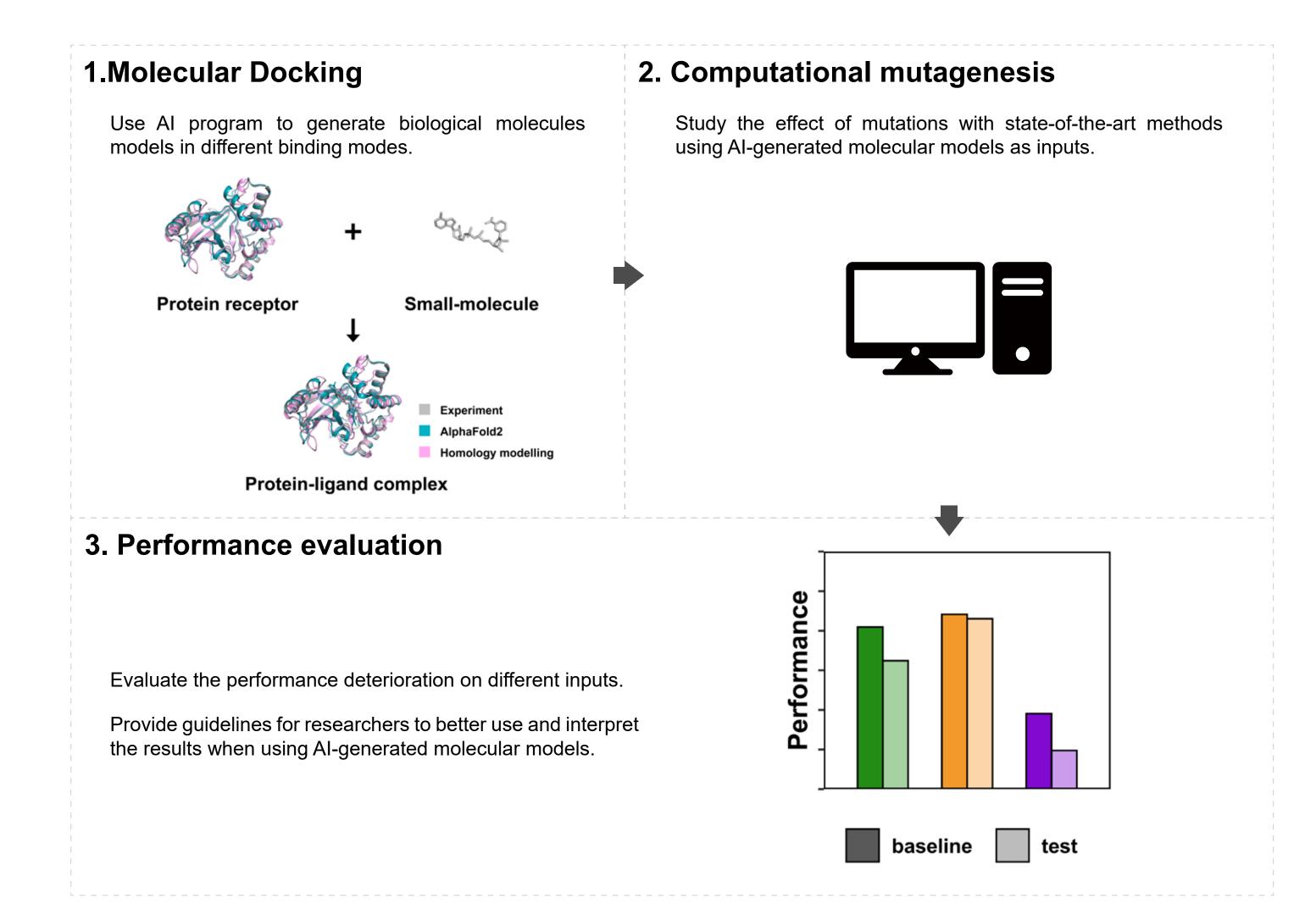
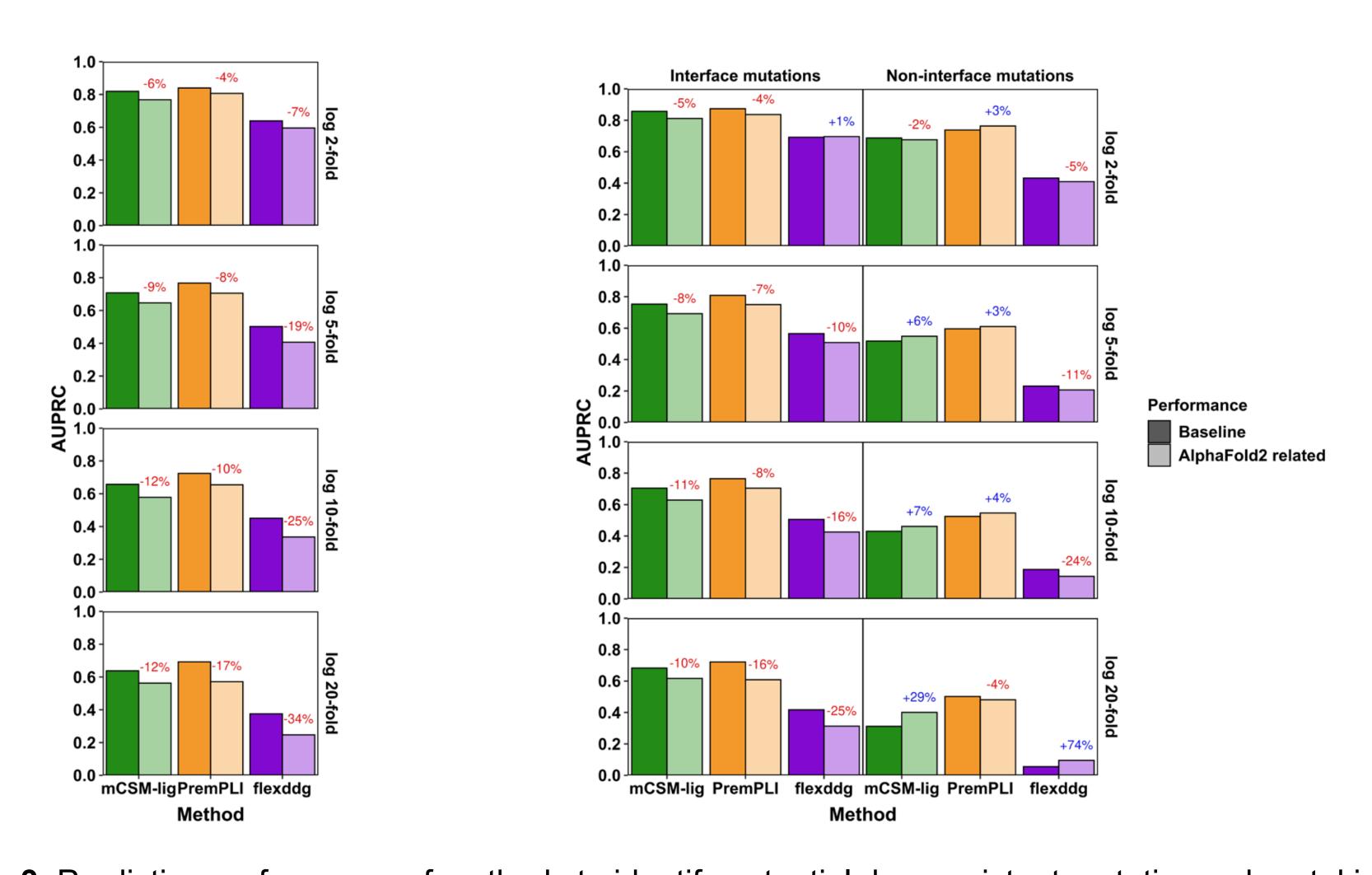


Fig 2. Methodology: research analysis workflow

### Yes we can, but we need to pay attention to ...



**Fig 3.** Predictive performance of methods to identify potential drug resistant mutations when taking Al-generated molecules as inputs.

- •In this work, we observed that there is ~15% performance deterioration for the current methods when using AlphaFold2-based molecules as inputs to identify potential drug-resistant mutations.
- This consistent performance deterioration could also be observed in different biochemical properties of receptors, such as interface mutations.

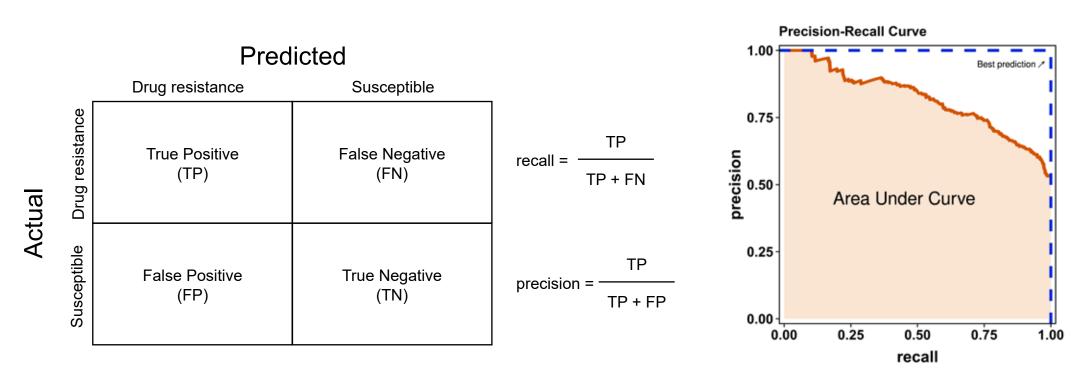


Fig 4. Area Under Precision-Recall Curve (AUPRC)

#### Potential application

• This work could provide **fundamental guidelines** for better interpretation on the predictions of current methods when using AI-generated protein-ligand complexes as inputs to characterise potential drug-resistant mutations, which may provide new insights to improve drug efficacy.

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#### **Digitial poster**



#### Personal website



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