Deep Learning Approaches to improve Drug-Target Binding Affinity Prediction in Precision Oncology

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Abstract

In precision oncology, it's important to understand how **mutations** change drug binding. We used the **generative model Boltz-2** to study the **epidermal growth factor receptor (EGFR)** a protein on the cell surface that controls growth and is often mutated in cancers such as lung cancer. Our benchmarking found key regions that influence how drugs bind, highlighting how **generative models** can be used to study mutation effects. This work opens insights for further benchmarking to better understand the role of generative models in **drug–target binding**.

Objectives

- Use **deep learning** to predict EGFR drug binding for different structural changes.
- **Identify protein regions** most important for drug binding through truncation experiments.
- **Test** how **mutations** in these key regions **affect** predicted drug binding.
- **Benchmark generative models** for their ability to study protein flexibility and drug response, highlighting their potential in guiding experimental research.

Reference : Passaro S, Corso G, et al. (2025) Boltz-2: Towards Accurate and Efficient Binding Affinity Prediction

Methodology

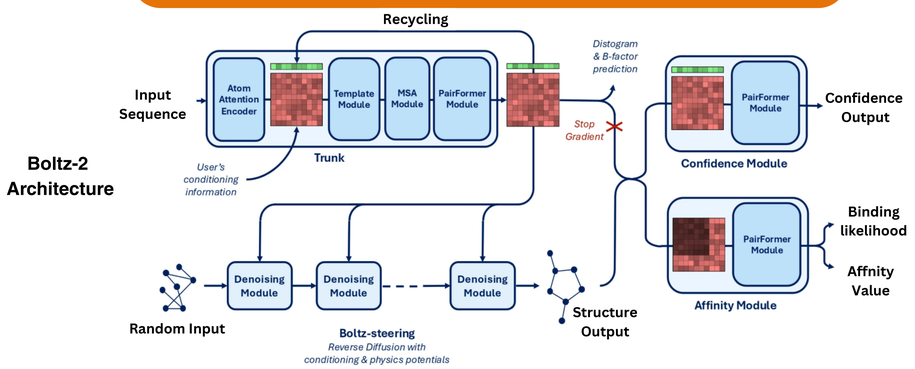
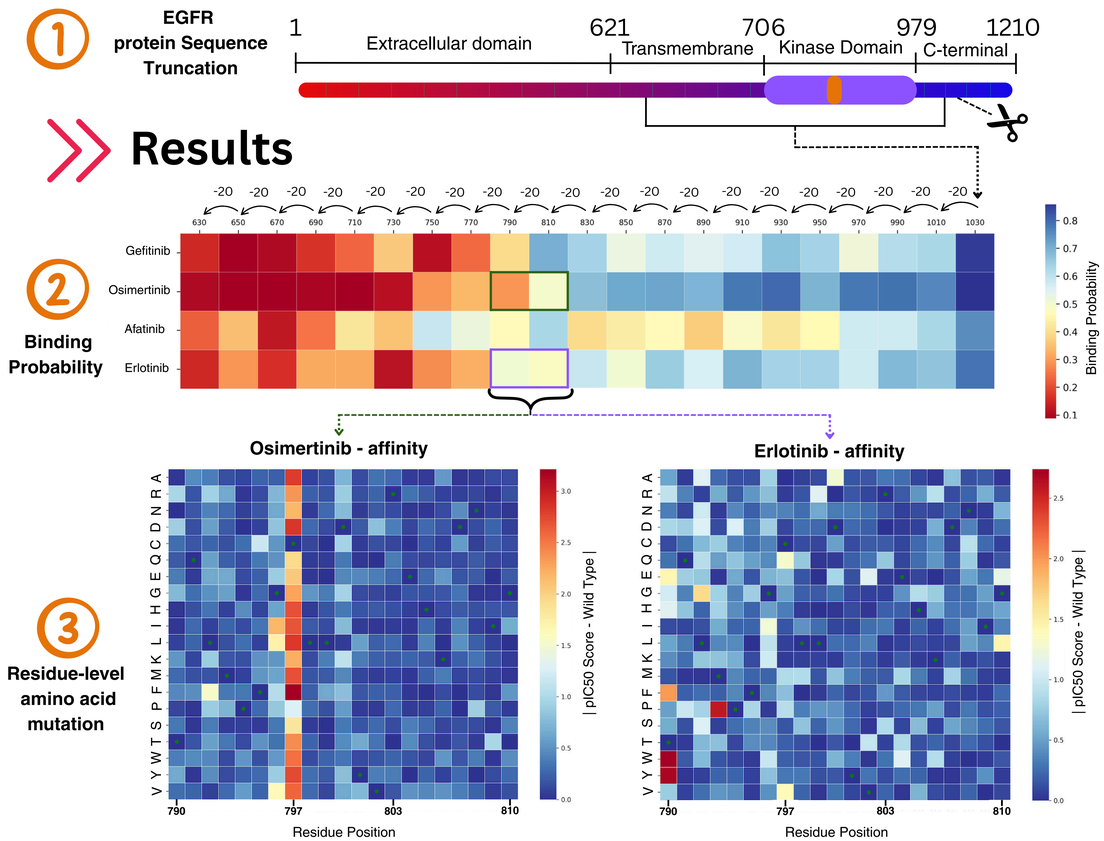


Figure 2. Boltz-2 model architecture (Passaro et al., 2025).

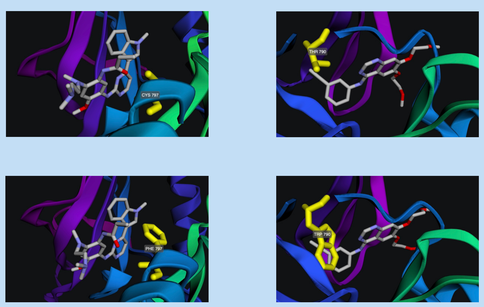
Results



Conclusion

This early **benchmarking** study opens insights into how **generative models** like **Boltz-2** can simulate structural changes in EGFR and explore their effects on **drug-binding**. Our pipeline can be extended to more drugs and mutation scenarios, helping researchers **prioritize** candidate treatments for specific mutation profiles. This approach has the potential to support more personalized drug selection strategies and **guide targeted laboratory testing**, highlighting the growing role of generative models in precision oncology.

EGFR–Drug Binding Poses



More info

3D Visual