# Pose Prediction Using Boltz-1 for the ASAP Polaris Challenge

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**Abstract**

The Report is part of our submission for the **ASAP Discovery** - Antiviral Ligand Poses 2025 challenge hosted by Polaris. The challenge is a collaborative effort aimed at enhancing computational methods for predicting ligand poses in antiviral drug discovery. Accurate prediction of ligand binding poses is crucial for understanding molecular interactions and developing effective therapeutics. This report details the application of Boltz-1, an open-source deep learning model, to predict ligand poses as part of the challenge.

## 1 Introduction

**Boltz-1** is an open-source model designed to predict the 3D structures of biomolecular complexes, including proteins, RNA, DNA, and small molecules [1]. The advantage over commercial tools its is ease of use and ability to use any small molecule ligands in a co-folding setting and not just predefined ones through a server.

# 2 Methodology

## 2.1 Data Preparation and Implementation

The dataset provided by the ASAP Polaris Challenge included sequences for chains A and B, as well as the corresponding CXSMILES. Additionally, the dataset contained complex structures of MERS-CoV Mpro and SARS-CoV-2 Mpro, along with their corresponding ligands, but these were available only for the training set.

For our analysis, we generated FASTA files using the sequences from chains A and B and the CXSMILES. These files were then input into Boltz-1 for inference. The inference was run on a single Nvidia T4 GPU.

## 2.2 Post Prediction

First, we used PyMOL to align the predicted complexes with the provided reference complexes and then extracted the ligand structures as .mol2 files.

We discovered that the predicted ligands were missing bond order information, which prevented them from passing the evaluation pipeline. To resolve this, we wrote a script to transfer bond order information from the SMILES representation to the predicted structure.

For the first 100 data points in the training set, approximately 40 of the predicted ligand poses had an RMSD of less than 2 Å from the true pose.

We did a small test with the first 100 datapoints of the training set but ultimately, we did not utilise the training data ( e.g fine-tuning) and submitted vanilla predictions using open-source model and weights of Boltz-1.

Using the same pipeline — Boltz-1 prediction followed by bond order transfer — we generated our submission for the test set. Our implementation is available on our Polaris Challenge Github Repo under the 'pose' submodule. The submodule for transferring bond order from reference SMILES to predicted structure code is also independently available at MolReBond repo

# 3 References

# References


[1] J. Wohlwend et al., "Boltz-1: Democratizing Biomolecular Interaction Modeling," *BioRxiv*, 2024. Available: https://www.biorxiv.org/content/10.1101/2024.11.19.624167v1

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[3] J. Wohlwend, "Official Boltz-1 GitHub Repository." Available: https://github.com/jwohlwend/boltz