Docking Validation and Virtual Screening for 6A93 Receptor

Project Overview

This repository contains the workflows, scripts, and validation results for a molecular docking study focused on identifying potential ligands targeting the 6A93 receptor, which has been implicated in depression and neuropsychiatric disorders.

The project aims to:

- Validate the docking protocol using a known co-crystallized ligand.

- Perform virtual fishing (screening) of potential ligands from various compound libraries.

- Identify high-affinity candidates for further in-silico and experimental evaluation.

Workflow Summary

1. Protein Preparation

- Receptor PDB ID: 6A93

- Source: [RCSB Protein Data Bank](https://www.rcsb.org/structure/6A93)

- Processed using Schrödinger Maestro’s Protein Preparation Wizard:

- Added hydrogens and optimized hydrogen bonds.

- Assigned bond orders and protonation states.

- Minimized with the OPLS4 force field.

- Retained key water molecules mediating ligand interactions.

2. Ligand Preparation

- Co-crystallized ligand extracted and prepared using LigPrep:

- Protonation states generated at pH 7.0 ± 2.0.

- Geometries minimized (OPLS4).

- Additional ligand libraries prepared for screening (see `data/ligands/`).

3. Receptor Grid Generation

- Grid centered on the active site defined by the co-crystallized ligand.

- Grid size: default (inner box 10 Å, outer box 20 Å).

- Grid generated via Receptor Grid Generation panel in Maestro.

4. Docking Validation

- Conducted redocking of the co-crystallized ligand.

- Aligned docked pose with the experimental pose to calculate RMSD.

- Validation Metrics:

- Method: Maximum Common Substructure (MCS)

- RMSD: `1.9797 Å` ✅ (Validated protocol)

- Max Difference: `4.4615 Å` between atoms 15 & 15

- Validation confirmed the reliability of the grid and docking parameters.

5. Virtual Fishing / Screening

- Docking of candidate compounds performed using Glide SP and XP modes.

- Scoring metrics include:

- GlideScore

- Emodel

- Binding Energy (post-docking MM-GBSA)

Repository Structure

Key Tools and Software

- Schrödinger Maestro (Protein Prep, Glide, SiteMap, Prime)

- Python for data parsing and analysis

- R for visualization of docking scores and hit distributions

📈 Validation Outcome

✅ The docking protocol achieved an RMSD of 1.98 Å, confirming the accuracy of the binding site definition and grid generation process.

This validated setup was subsequently used to screen novel ligands with potential antidepressant or neuroprotective properties.

🧪 Next Steps

- Perform MM-GBSA rescoring on top-ranked ligands.

- Investigate pharmacokinetic and ADMET properties.

- Conduct molecular dynamics simulations on selected hits.

**Author**

**Dr. Samuel Amoako (PharmD, MPSGh)**

**Neuropharmacology and Drug Discovery Researcher**

**University of Cape Coast, Ghana**

**sammieamoako@gmail.com**

**[LinkedIn](https://www.linkedin.com/in/dr-samuel-amoako-pharmd-330b301b0) | [GitHub](https://github.com/sammieamoako)**

**Citation**

**If you use this workflow, please cite this repository as:**

**> Amoako S. (2025). Docking Validation and Virtual Screening for 6A93 Receptor in Depression and Mental Disorders. GitHub Repository.**

**> [https://github.com/sammieamoako/6A93-Docking-Validation](https://github.com/sammieamoako)**

**Disclaimer**

**This project is part of a research initiative aimed at exploring drug–receptor interactions for academic purposes.**

**It is not intended for clinical or diagnostic use.**