Computational Drug Design

Molecular Docking of Lopinavir with HIV-1 Protease

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Project Context

- High-school research project at Shanghai Foreign Language School Affiliated to SISU, Minhang Foreign Language School.
- Topic: molecular docking between lopinavir and HIV-1 protease.
- Toolchain: Schrödinger Maestro, receptor preparation, ligand preparation, Glide docking.
- Outcome: First Prize, 2021 Shanghai Youth Science and Innovation Workstation Competition.

Research Question

How can molecular docking model the interaction between lopinavir and HIV-1 protease, and how do grid settings affect the predicted binding pose?

Biological Motivation

- HIV protease processes viral precursor proteins into mature viral components.
- Protease inhibition can disrupt viral maturation.
- Lopinavir is a peptidomimetic HIV protease inhibitor.
- Docking provides a computational way to inspect candidate binding poses before experimental work.

Computational Workflow

1. Prepare lopinavir 2D and 3D structures.
2. Prepare and optimize HIV-1 protease from PDB 1MIU.
3. Generate docking grids at 15, 18, and 20 Å.
4. Dock lopinavir into the receptor.
5. Rank poses by Glide GScore.
6. Interpret hydrogen-bond, hydrophobic, and electrostatic interactions.

Best Pose by Grid Size

Grid size	Best conformation	Glide GScore
15 Å	LOP_15_1	-10.758
18 Å	LOP_18_1	-11.898
20 Å	LOP_20_1	-10.192

The strongest reported docking score came from the 18 Ågrid.

Interaction Interpretation

- 15 Å: hydrogen bonds involving Ash25 and Ile50, plus possible electrostatic and hydrophobic contacts.
- 18 Å: reported as the most stable pose, with seven hydrogen bonds and contacts near Ile50, Ash25, Leu23, Ala28, and Val32.
- 20 Å: top pose interpreted mainly through electrostatic interactions near acidic residues.

Limitations

- Docking score is not experimental validation.
- Results depend on receptor preparation, protonation state, grid definition, and force-field settings.
- No molecular dynamics or free-energy calculation was included.
- The project is best read as early computational-modelling training.

What This Demonstrates

- Literature-based framing of a biomedical modelling question.
- Use of professional molecular-modelling software.
- Quantitative comparison of docking outputs.
- Qualitative interpretation of molecular interactions.
- Awareness that computation needs validation before scientific claims are made.