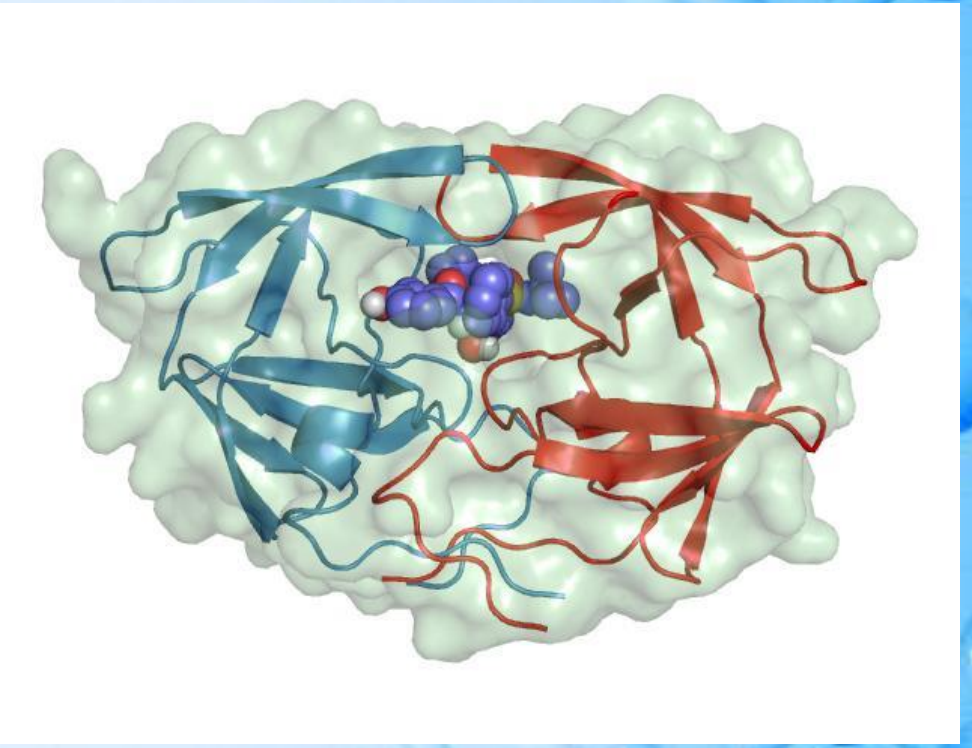
Molecular Docking Mini Project



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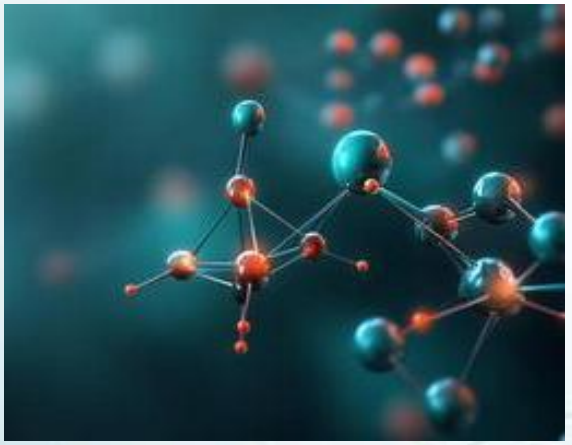
Introduction:



Molecular Docking: What Is It?

A computer based technique called molecular docking is used to forecast how a small molecule, or ligand, will fit into a target protein's active site.

Drug design benefits from knowing the kind and strength of the interaction between the ligand and protein.

About SARS-CoV-2 Main Protease (Mpro)

The virus responsible for the COVID-19 pandemic is SARS-CoV-2.In order to convert viral polyproteins into functional proteins required for virus replication, the Main Protease (Mpro) is essential.

Mpro is a promising therapeutic target because it can be inhibited to stop viral replication.

About Catechin Gallate (ligand)

Green tea contains a naturally occurring substance called catechin gallate , which is categorized as a flavonoid. Its antiviral, antioxidant, and health promoting qualities are well known. According to scientific research, it may inhibit viral proteins and be a viable treatment option for COVID-19.

Research Objectives:

1. Tools for Software

- PyMOL: A tool for preparing and visualizing ligand and protein structures
- MMV(Molecular Modeling Visualisation): For the analysis and visualization of structures.
- Cao Lab Tools: For preparing proteins and ligands.

2. Online Databases

- RCSB Protein Data Bank (PDB) – To download the 3D structure of the target protein (SARS-CoV-2 Mpro)
  Example PDB ID: 6LU7
- PubChem – To download the 3D structure of the ligand (Catechin Gallate).

Step 1: Downloading Protein Structure Files

1.Navigated to RCSB PDB

I opened the Protein Data Bank website: [https://www.rcsb.org/] and searched for PDB ID: 6LU7 (SARS-CoV-2 Main Protease).

2.Located Target Structure

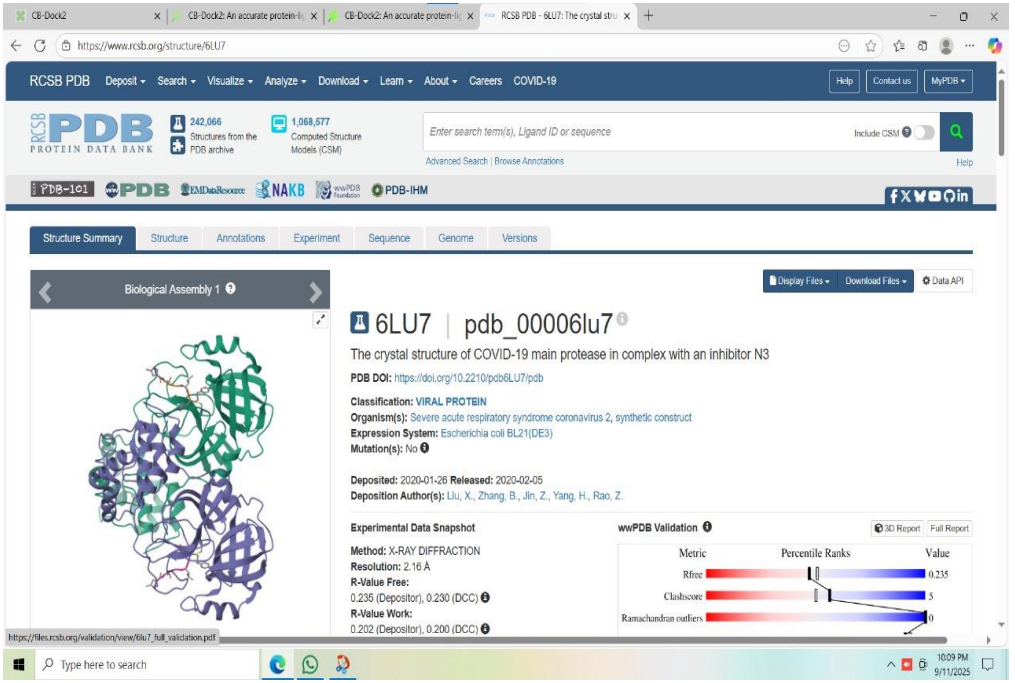
From the search results, selected the structure of SARS-CoV-2 Main Protease (Mpro) bound with an inhibitor.

3. Downloaded PDB File

Clicked on the “Download Files” option and selected PDB Format (.pdb) to download the protein structure file, which included protein coordinates.

4. Documented Process

Took a screenshot of the RCSB PDB website showing the 6LU7 page with the download options visible and saved it for the project report.



Step 2: Protein Preparation in PyMOL

1.Opened the Protein Structure

I opened the downloaded 6LU7.pdb file in PyMOL to visualize the protein structure.

2.Cleaned the Structure

Removed all non-standard residues and solvent molecules (HOH) present in the structure.

03. Removed Bound Ligand

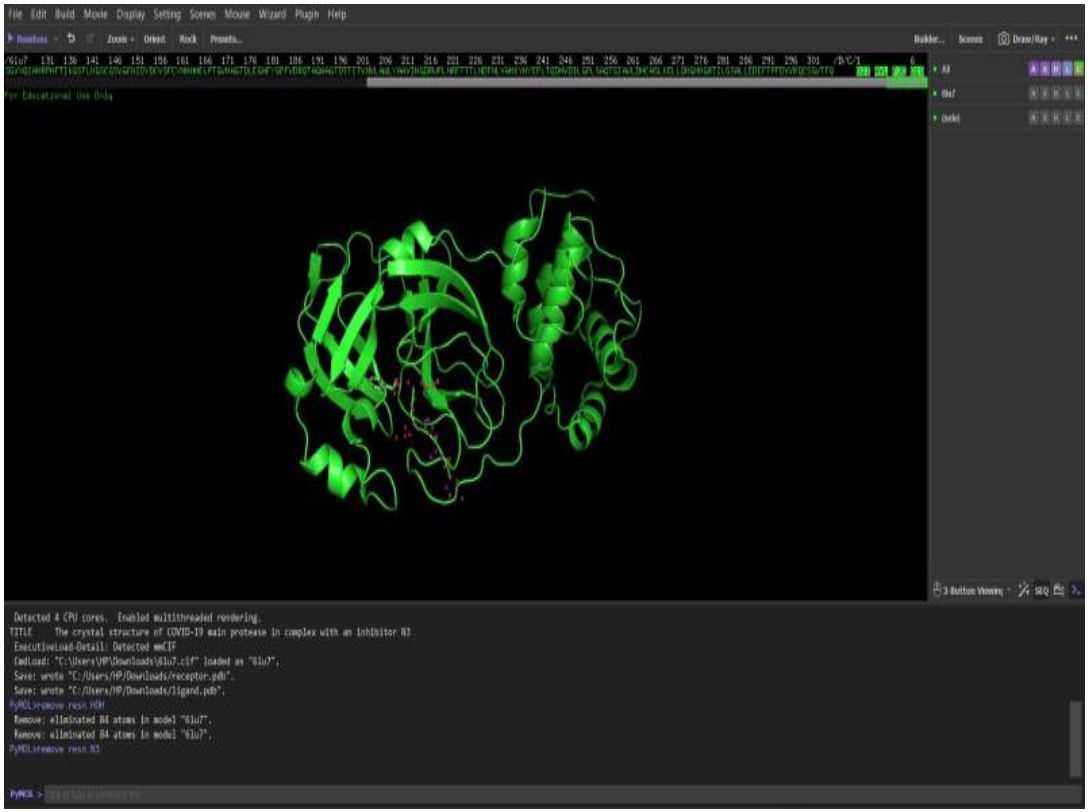
Carefully removed the bound ligand (if present) from the protein structure to prepare it for docking.

4. Added Hydrogens and Charges

Then added hydrogen atoms and assigned appropriate charges to the protein structure to make it ready for docking.

5. Saved the Clean Protein File

Finally, saved the prepared clean protein structure in .pdb format for the next docking steps.



Step 3: Ligand File Preparation

1.Accessed PubChem Database

Visited the PubChem database: [https://pubchem.ncbi.nlm.nih.gov/] and searched for Catechin Gallate (CID: 6419835).

2.Downloaded Ligand Structure

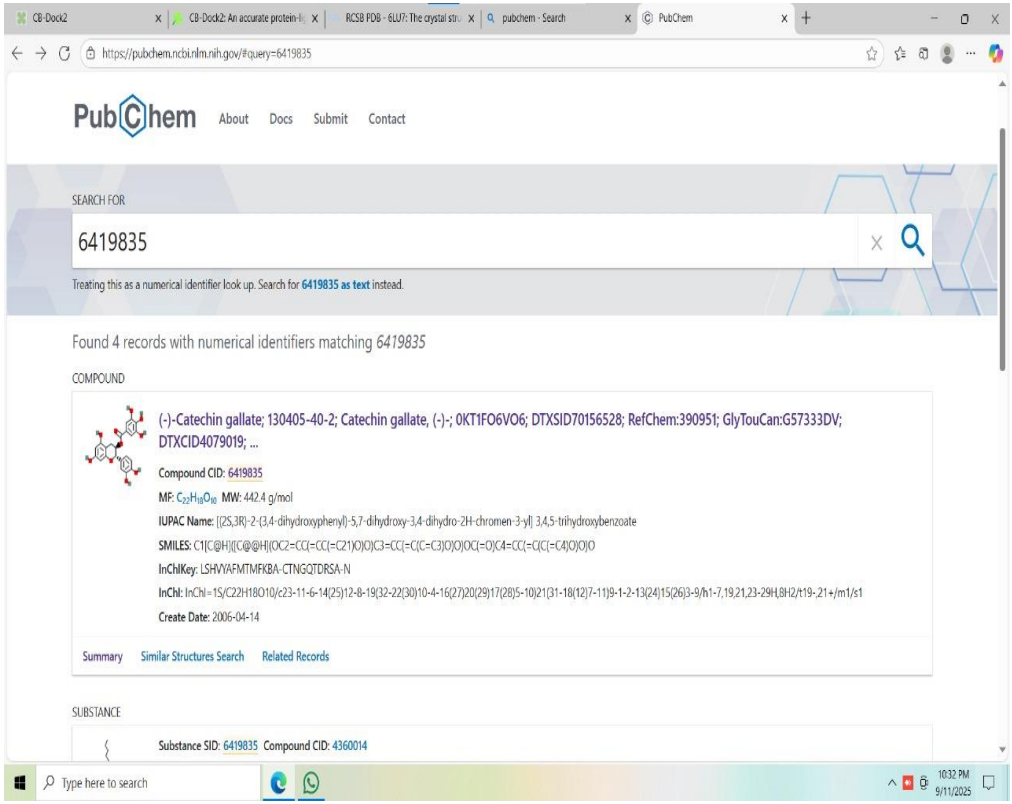
Then downloaded the 3D SDF structure file of Catechin Gallate for use in docking.

3. Prepared Ligand in PyMOL or Chimera

Opened the Catechin Gallate structure in PyMOL., added hydrogen atoms and assigned charges to the ligand. Since the ligand was stable, I skipped energy minimization.

4. Saved Clean Ligand File

Saved the prepared ligand file in .pdb format for the docking procedure.



Step 4: Executing Docking & Visualization

1.Selected Docking Platform

I used CB-Dock2 for the docking simulation.

2.Uploaded Files to CB-Dock2

Uploaded the prepared protein (.pdb) and ligand (.pdb) structure files.

3. Ran Docking Simulation

Ran the blind docking option, and CB-Dock2 generated docking results automatically.

4.. Analyzed Docking Results

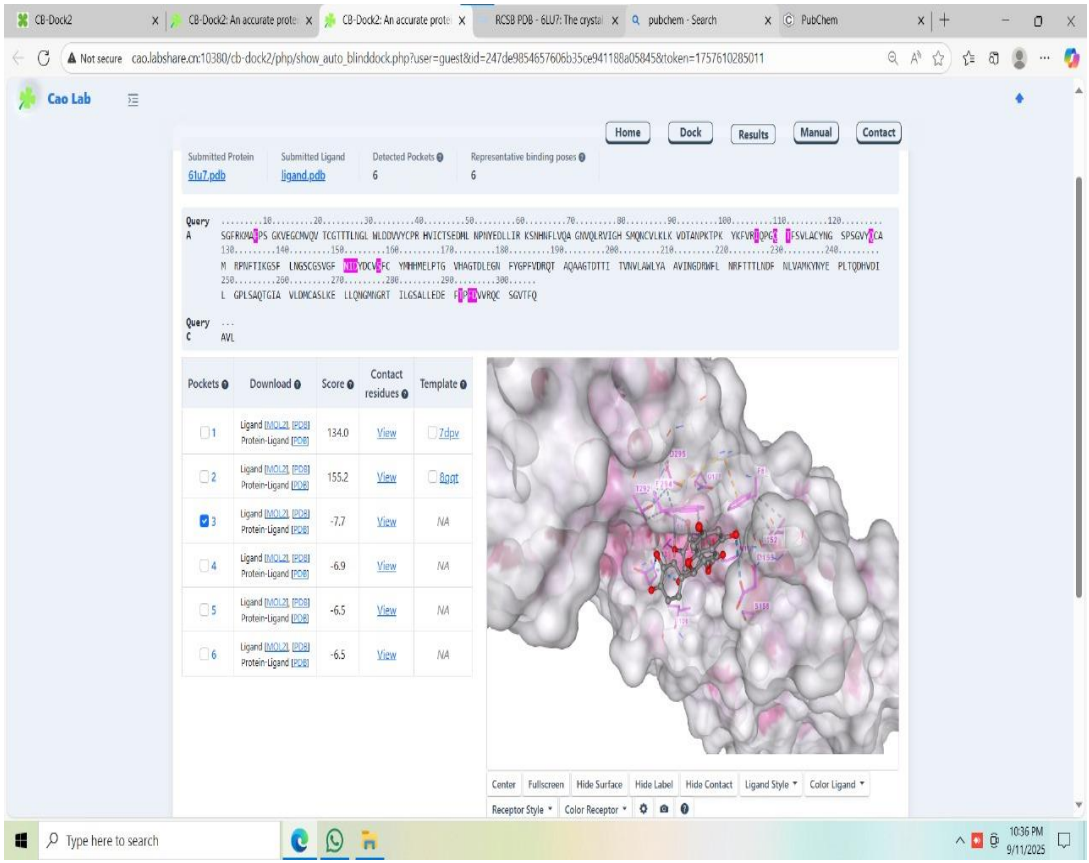
Downloaded the docking results showing multiple binding poses with scores.

Selected the best binding affinity result:

➔ Binding Energy = -7.7 kcal/mol

5. Visualized Docked Complex

Downloaded the docked protein-ligand complex structure for visualizing it in MMV.



Step 5: Complex Visualization & Interaction Mapping

1.Visualized Docked Complex in MMV

Opened the downloaded structure in MMV (Molecular Modeling Visualization) tool to examine the ligand's positioning within the protein active site.

2.Analyzed Binding Pose

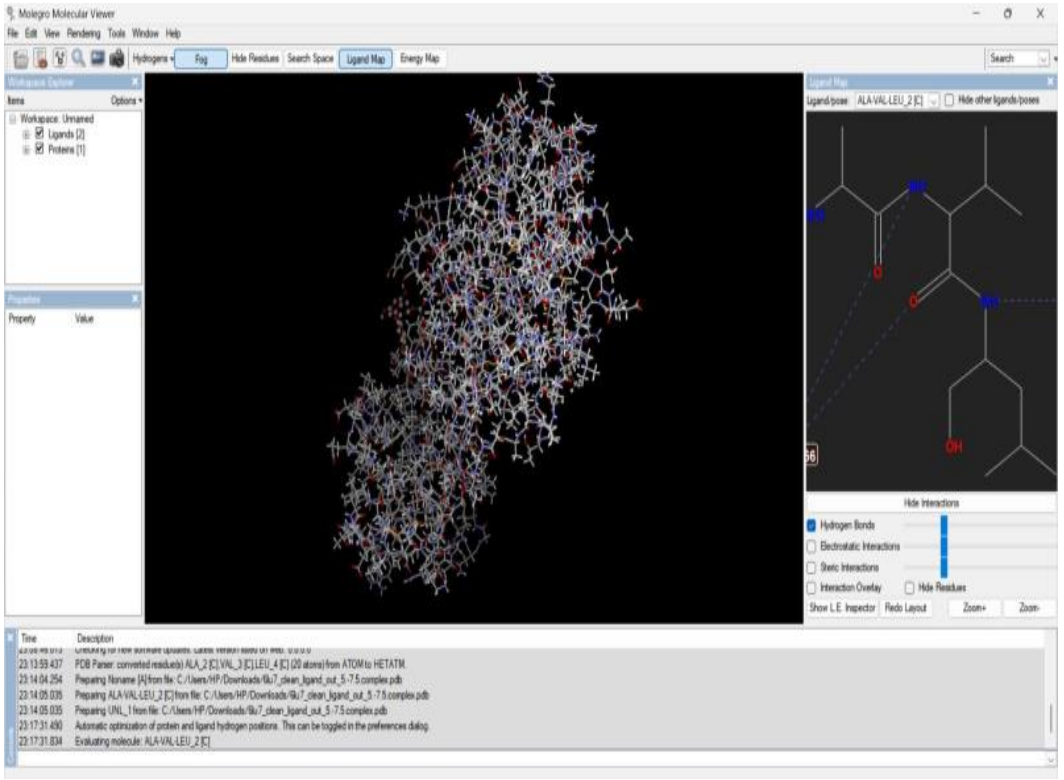
Confirmed that the ligand (Catechin Gallate) was properly positioned in the catalytic site (Binding Pocket) of SARS-CoV-2 Main Protease.

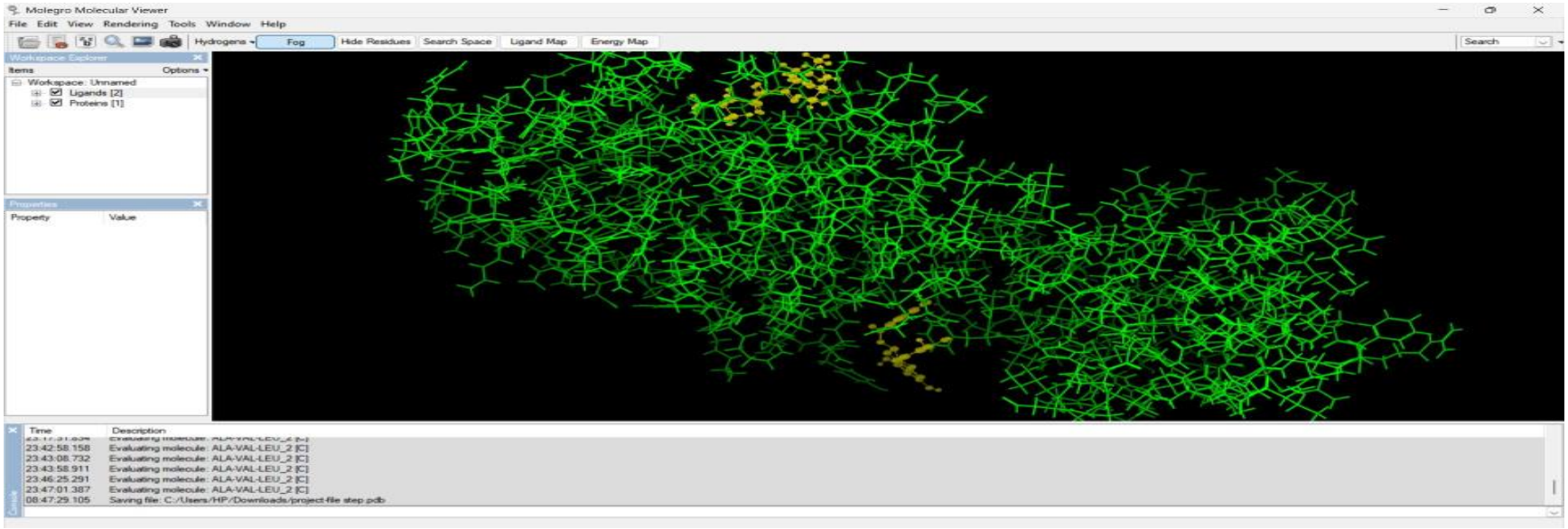
3. Performed Interaction Mapping

Identified important hydrogen bonds and hydrophobic interactions between the ligand and protein residues.

4. Enhanced Visualization

Then I applied different colour to distinguish the protein structure and ligand clearly. This visual confirmation ensured that the computational docking predictions aligned with chemical intuition and known binding mechanisms.





Conclusion

In this study, we successfully performed molecular docking of Catechin Gallate with the SARS-CoV-2 Main Protease (Mpro).

The results showed a significant binding affinity of -7.7 kcal/mol, indicating that Catechin Gallate has a good potential to interact with and inhibit the target protein.

Limitation

While the docking study provided useful insights, it is important to note that computational predictions are based on theoretical models. Actual biological activity and safety must be confirmed through laboratory experiments and clinical studies.