Ligands and Receptors: A Love Story

Binding Affinities Between Opioids and the μ-opioid Receptor

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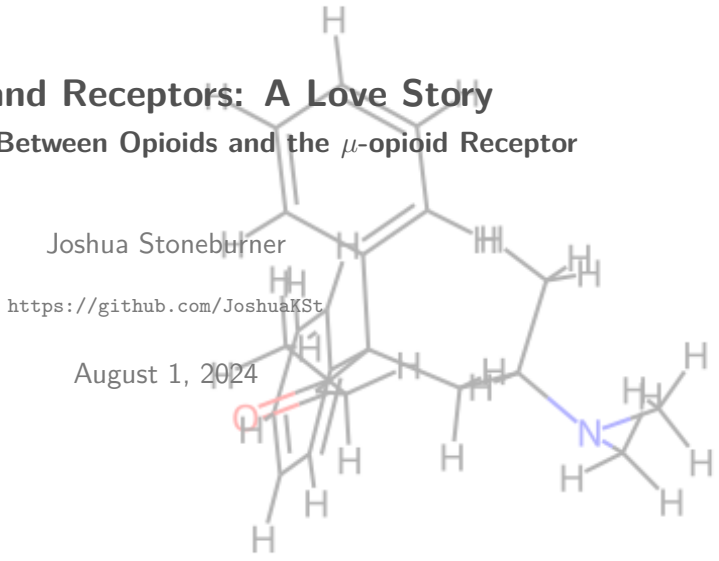
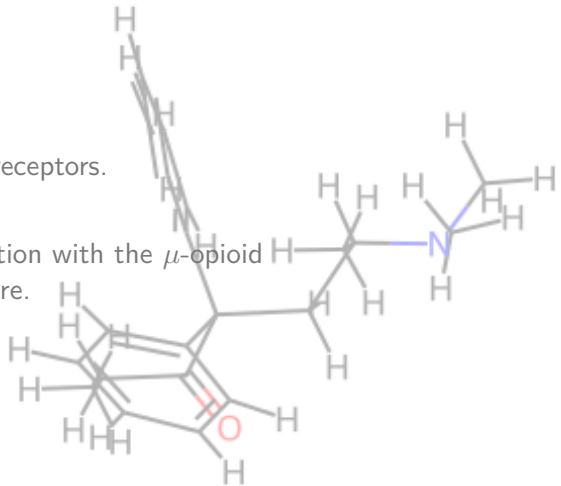
August 1, 2024



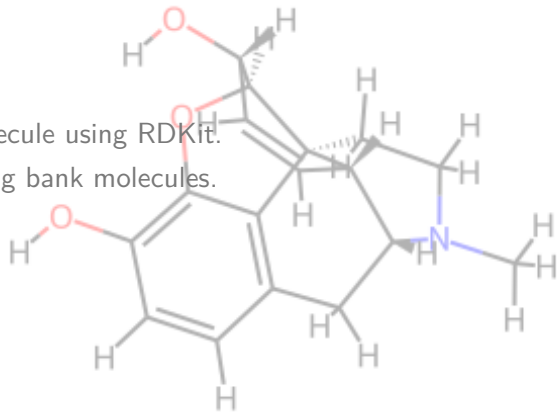
Research Goal

- Direction.
- Understand opioid receptors.
- Create a molecule.
- Simulate its interaction with the μ-opioid receptor and compare.

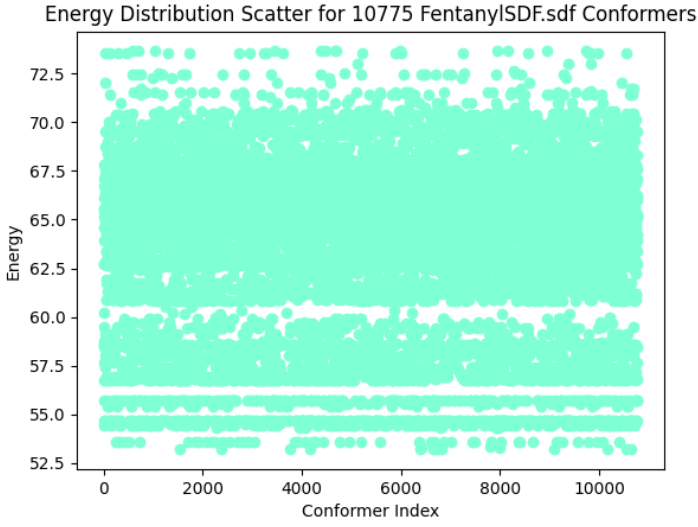


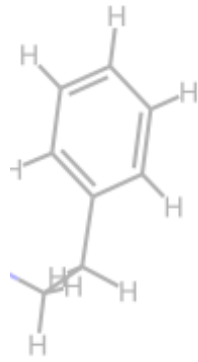
Molecule Creation and Optimization Method

- Generating the molecule using RDKit.
- Optimization of drug bank molecules.



Conformer Energy Graphs





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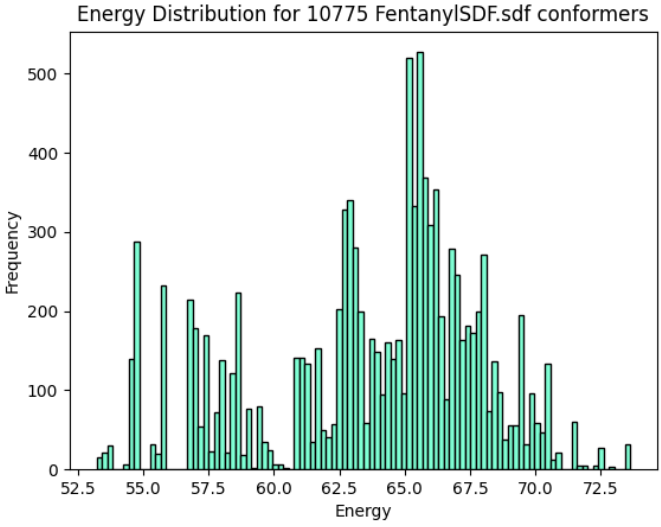

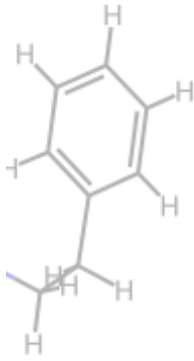

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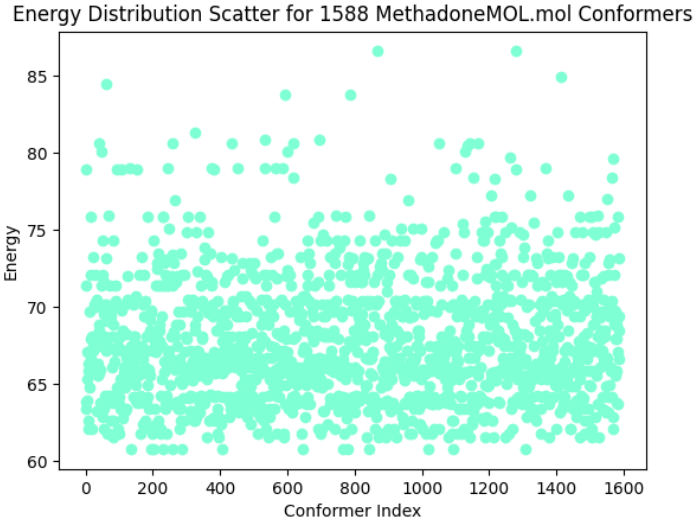

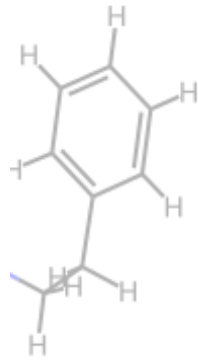

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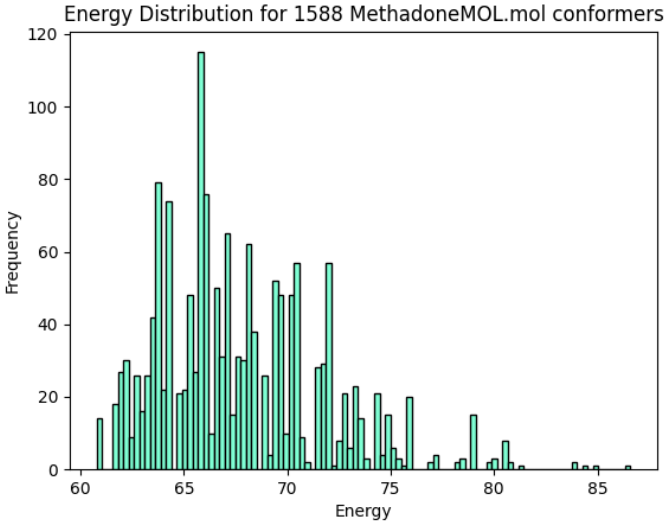

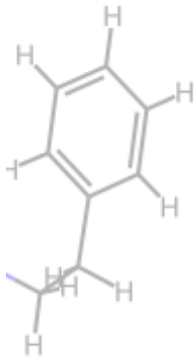

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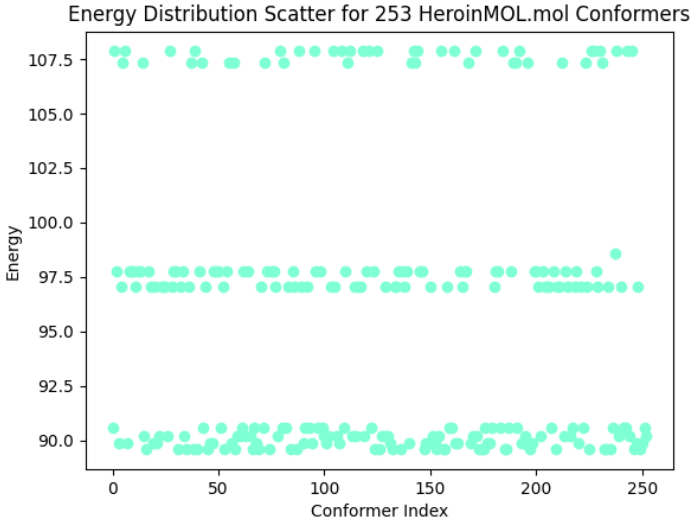

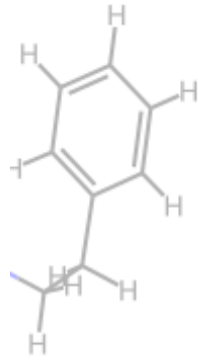

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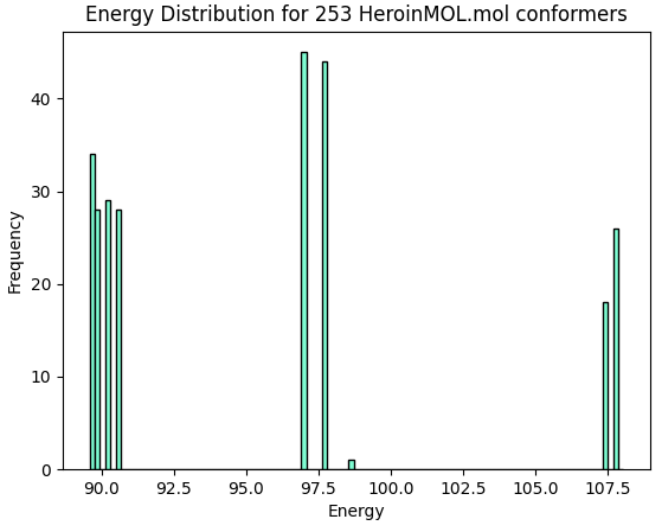
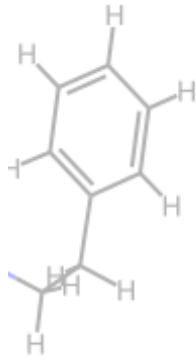
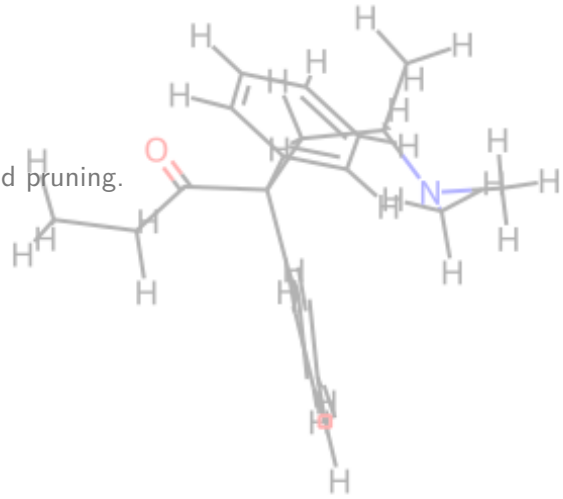




Experiment Setup

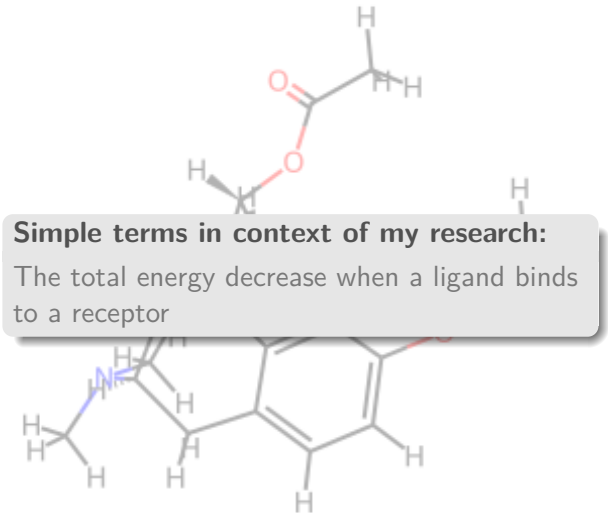
- Receptor finding and pruning.
- Simulate!



What are: "Binding Affinities"?

They are:

- How tightly bound an interaction is (i.e. a ligand and protein)
- Often referred to as the free energy of binding (ΔG)
- Used in drug optimization, computations of biological systems etc.

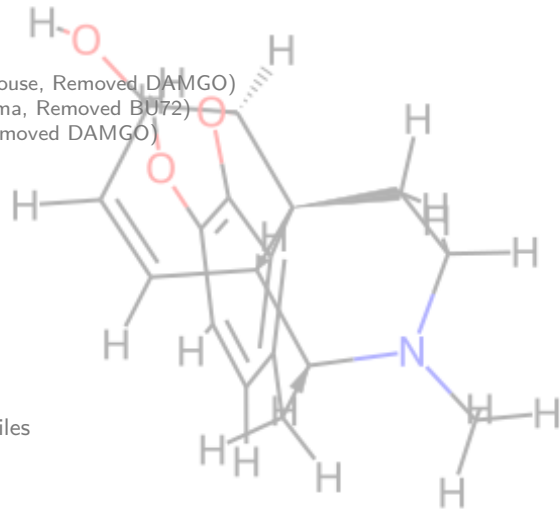


Simple terms in context of my research:

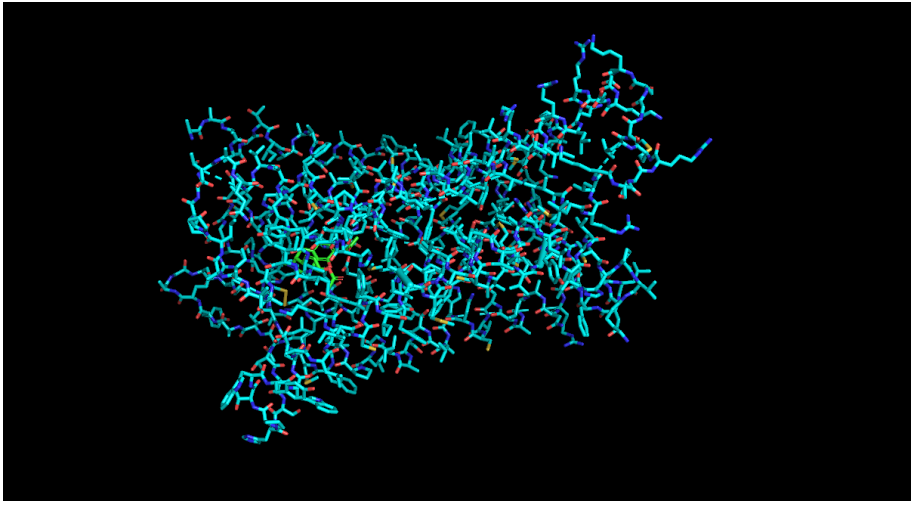
The total energy decrease when a ligand binds to a receptor

Briefing

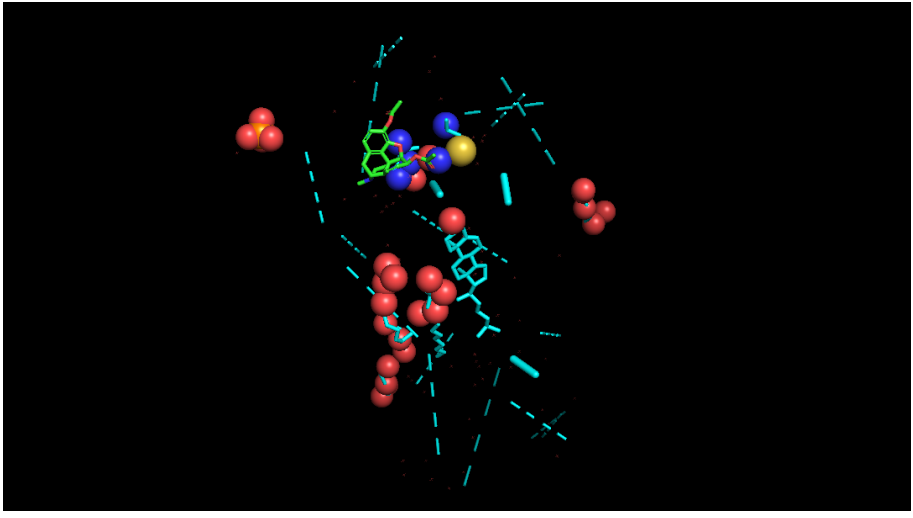
- μ-opioid Receptors
  - 6DDF (Human, Mouse, Removed DAMGO)
  - 8E0G (Mouse, Llama, Removed BU72)
  - 8K9K (Human, Removed DAMGO)
- Ligands
  - Heroin
  - Morphine
  - Fentanyl
  - Methadone
  - Carfentanil
  - BU72
- .SDF and .MOL
  - Structure Data Files



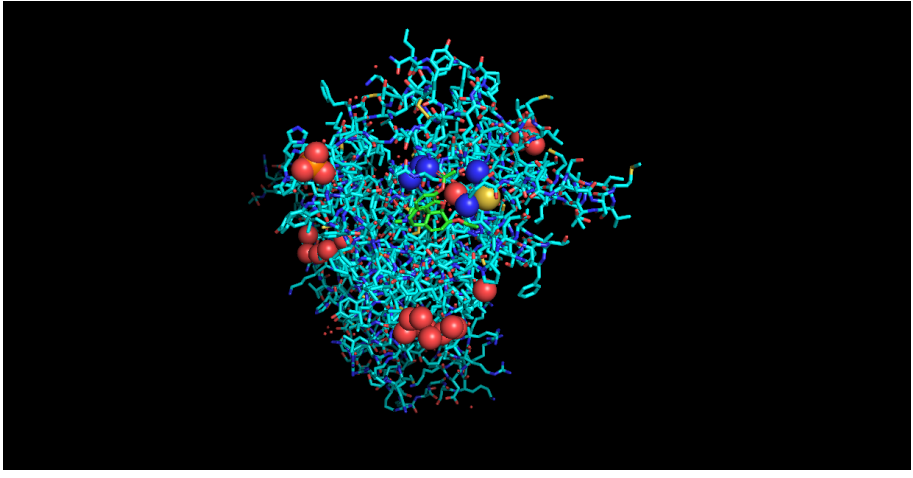
Heroin 6DDF Docking Output



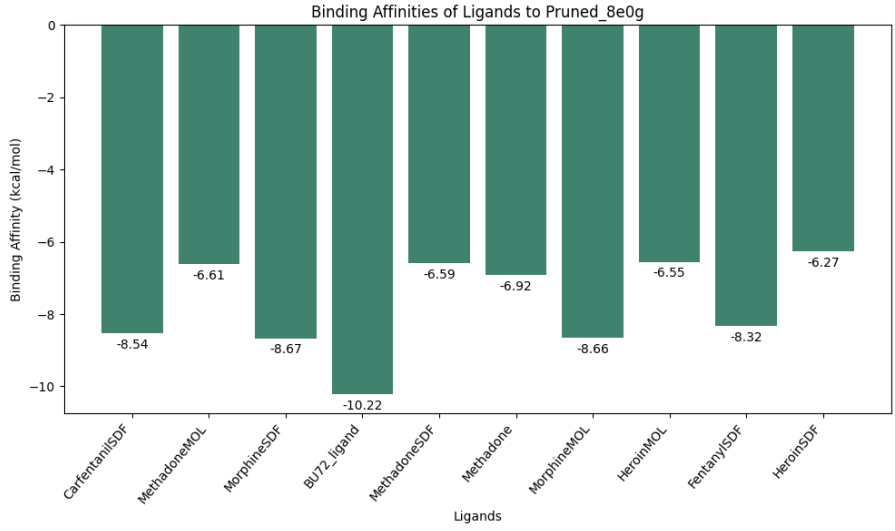
Heroin 8E0G Docking Output



Heroin 8E0G Docking Output



Affinity Graphs



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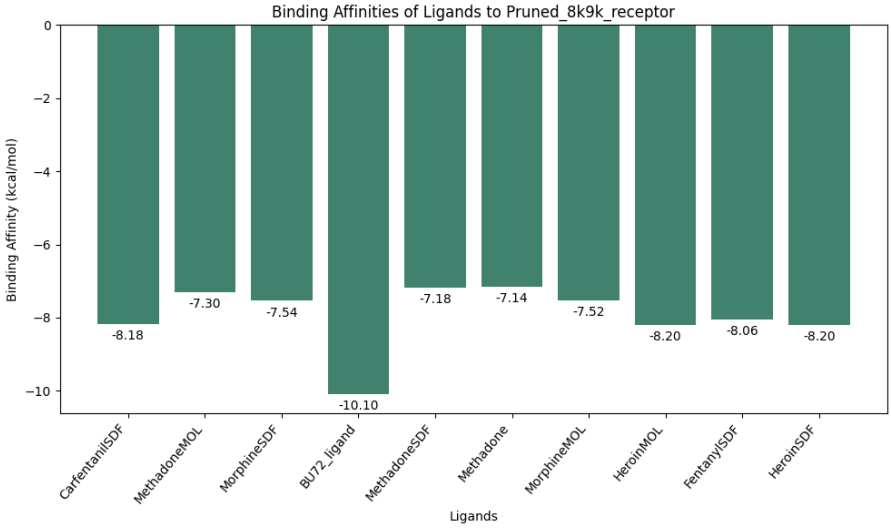

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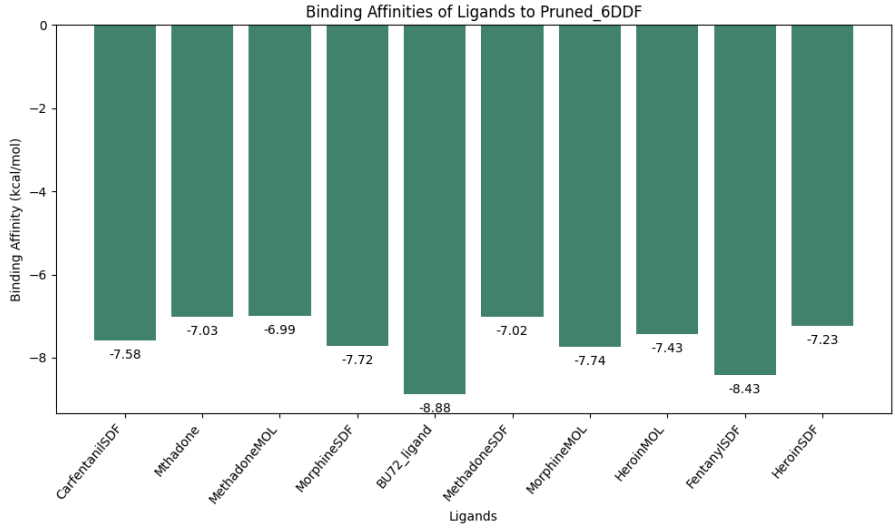
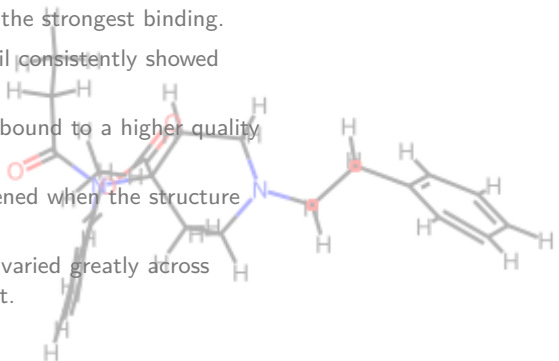


Analysis

- BU72 Consistently had the strongest binding.
- Fentanyl and Carfentanil consistently showed strong binding.
- Morphine was stronger bound to a higher quality model.
- The gap in affinity lessened when the structure was lower quality.
- Heroin and Methadone varied greatly across structure and file format.



Thank You!