

# Ligands and Receptors: A Love Story

## Binding Affinities Between Opioids and the $\mu$ -opioid Receptor

Joshua Stoneburner

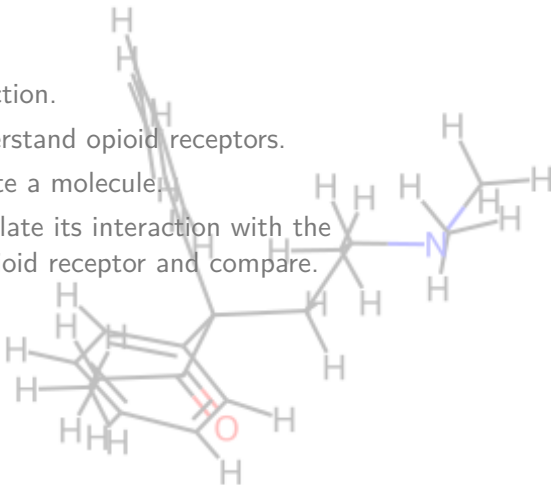
<https://github.com/JoshuaKSt>

August 1, 2024



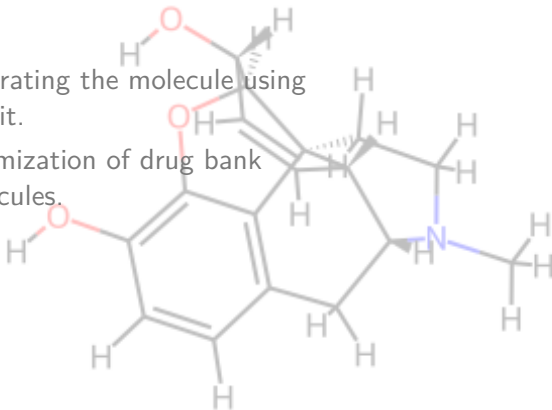
# Research Goal

- ▶ Direction.
- ▶ Understand opioid receptors.
- ▶ Create a molecule.
- ▶ Simulate its interaction with the  $\mu$ -opioid receptor and compare.

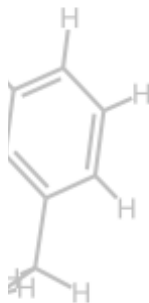
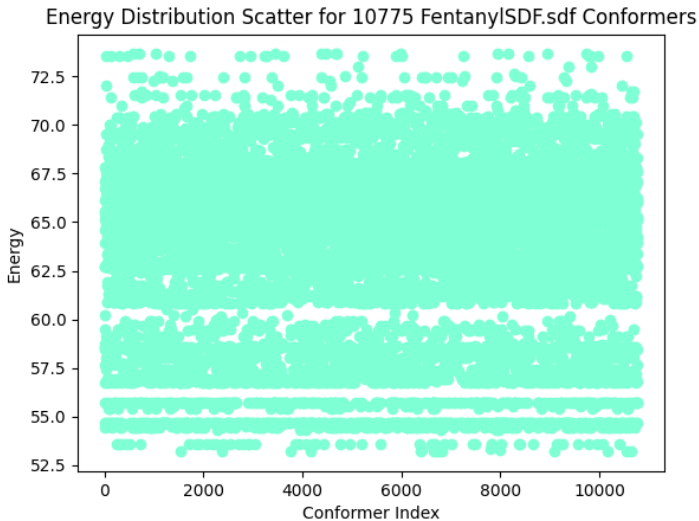


# Molecule Creation and Optimization Method

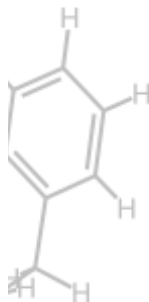
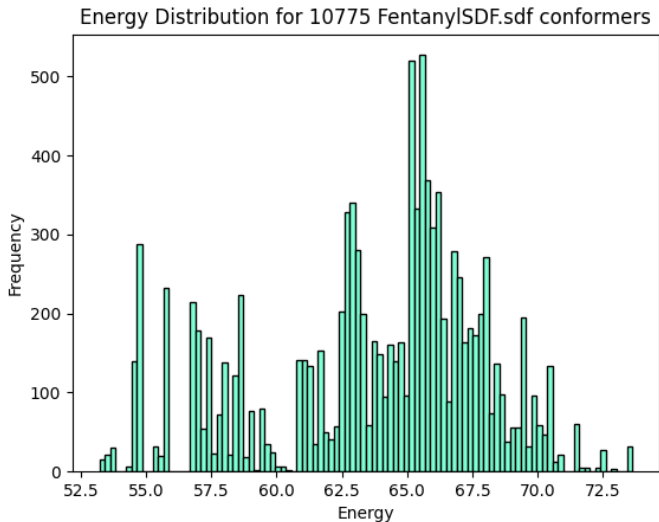
- ▶ Generating the molecule using RDKit.
- ▶ Optimization of drug bank molecules.



# Conformer Energy Graphs

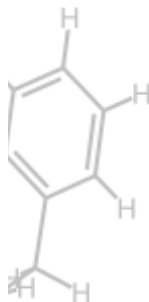
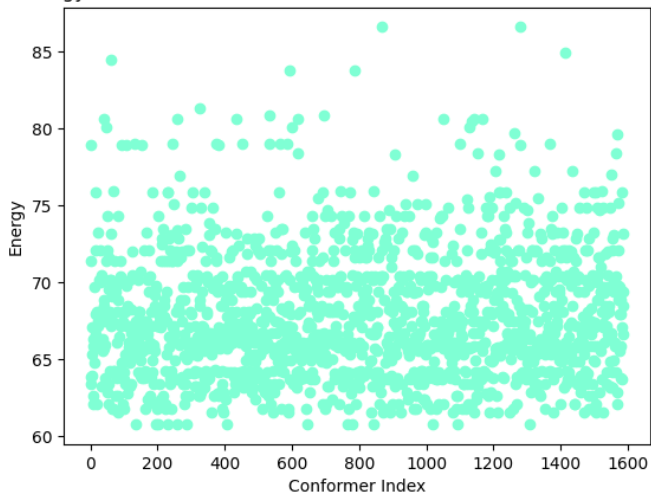


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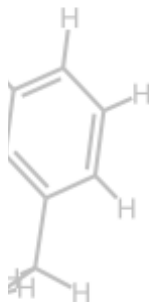
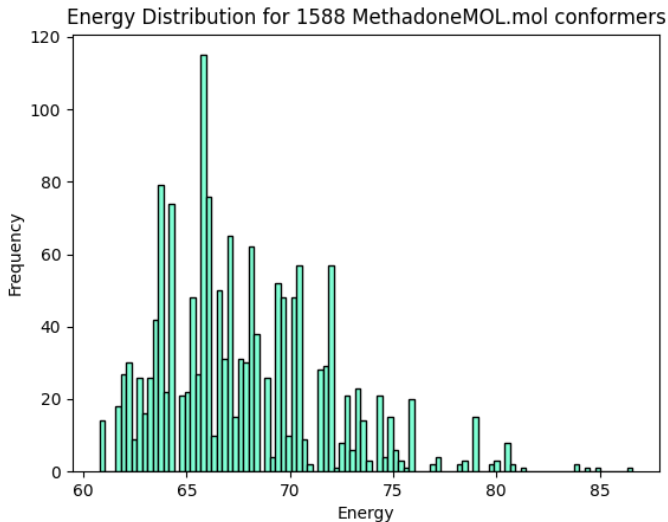


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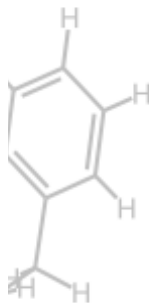
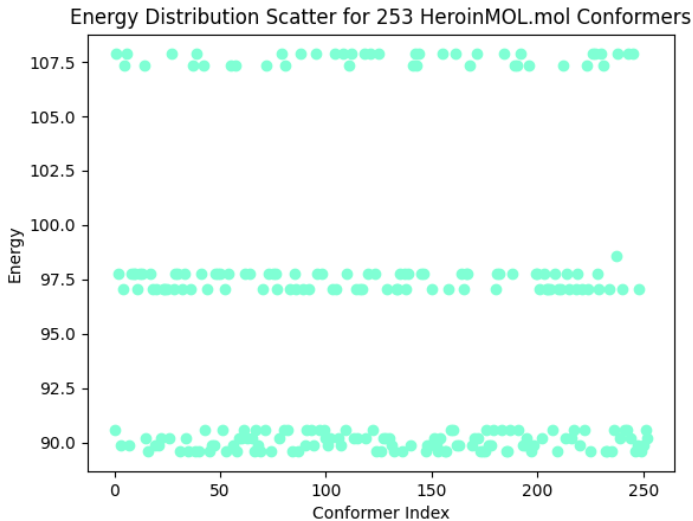
Energy Distribution Scatter for 1588 MethadoneMOL.mol Conformers



# Conformer Energy Graphs

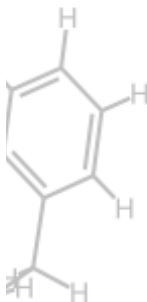
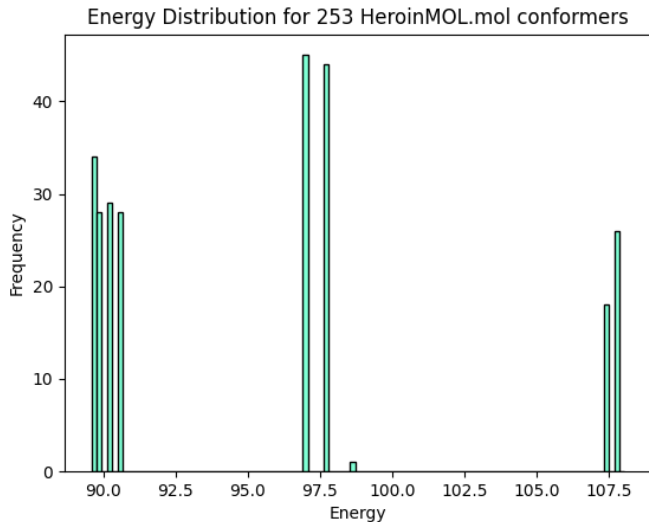


# Conformer Energy Graphs



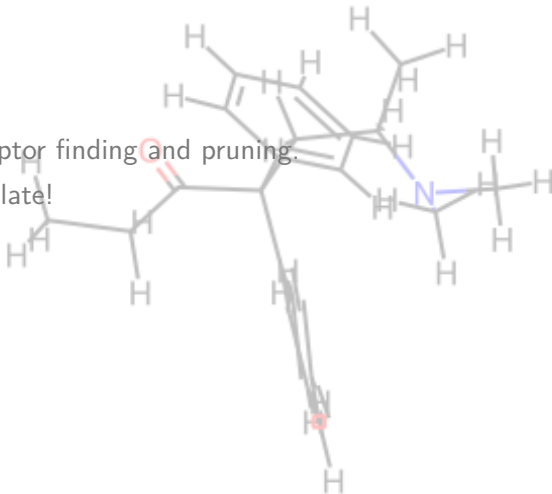


# Conformer Energy Graphs



# Experiment Setup

- Receptor finding and pruning.
- Simulate!



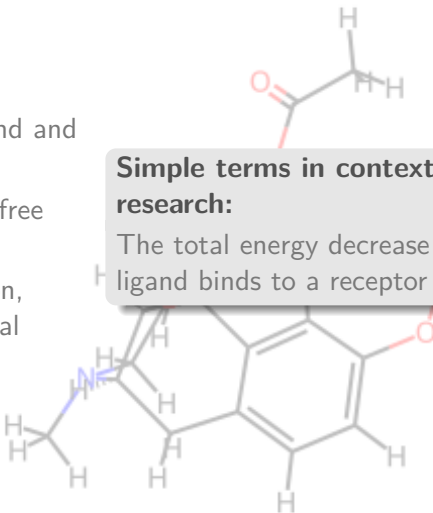
# What are: "Binding Affinities"?

They are:

- ▶ How tightly bound an interaction is (i.e. a ligand and protein)
- ▶ Often referred to as the free energy of binding ( $\Delta G$ )
- ▶ 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

## ► $\mu$ -opioid Receptors

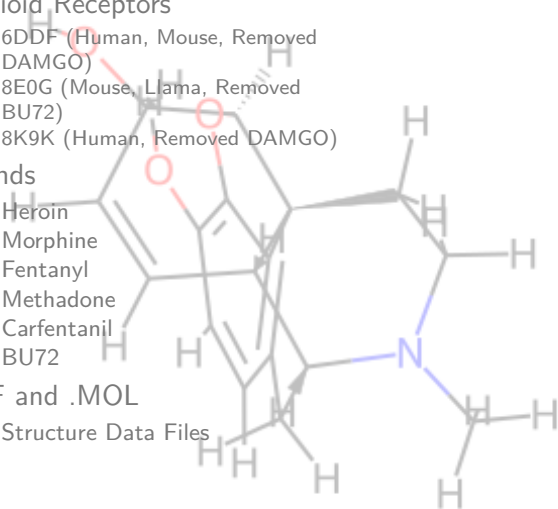
- 6DDF (Human, Mouse, Removed DAMGO)
- 8E0G (Mouse, Llama, Removed BU72)
- 8K9K (Human, Removed DAMGO)

## ► Ligands

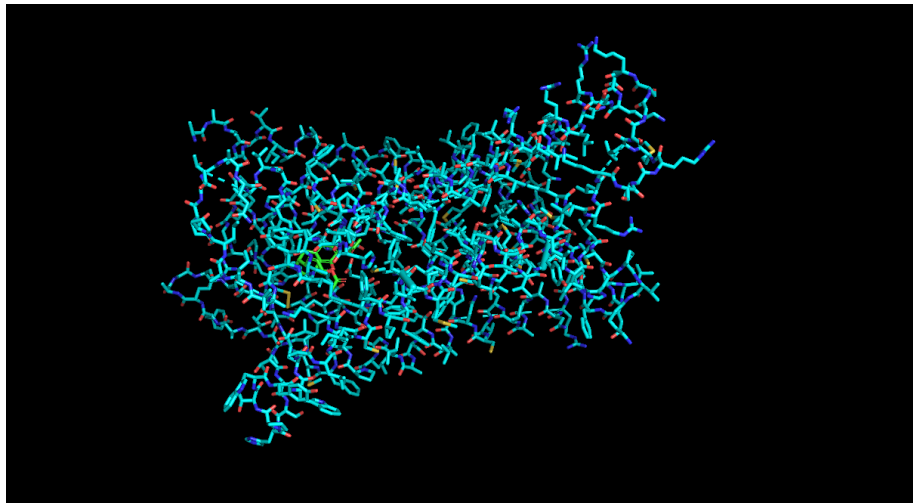
- Heroin
- Morphine
- Fentanyl
- Methadone
- Carfentanil
- BU72

## ► .SDF and .MOL

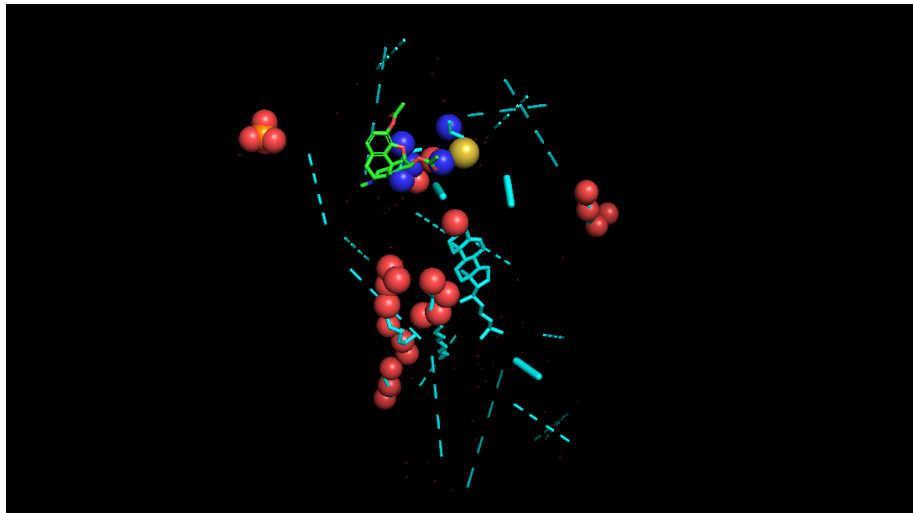
- Structure Data Files



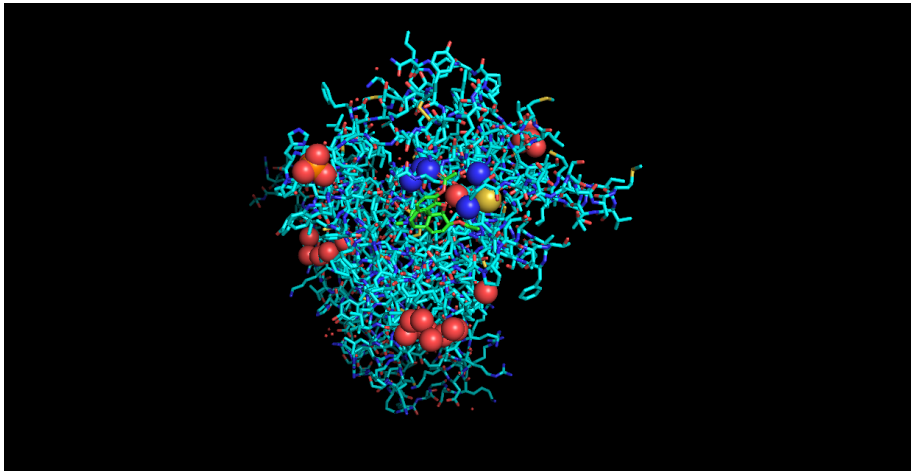
# Heroin 6DDF Docking Output



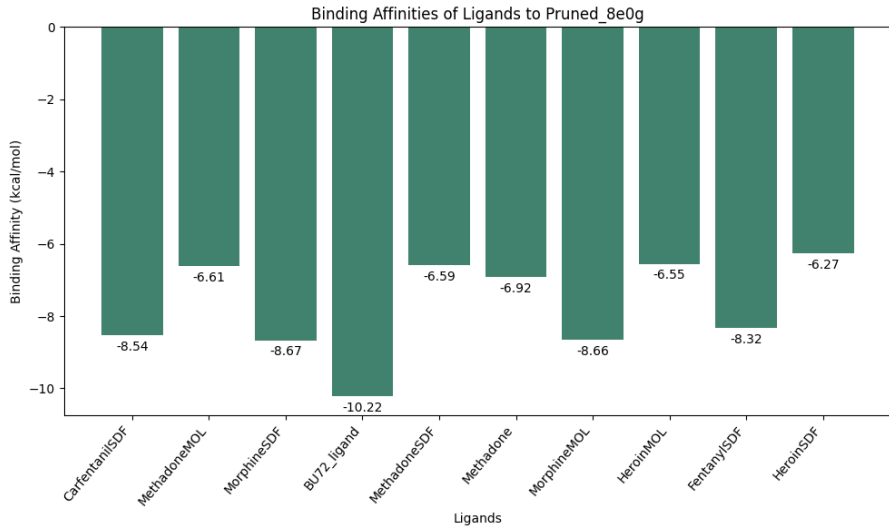
# Heroin 8E0G Docking Output



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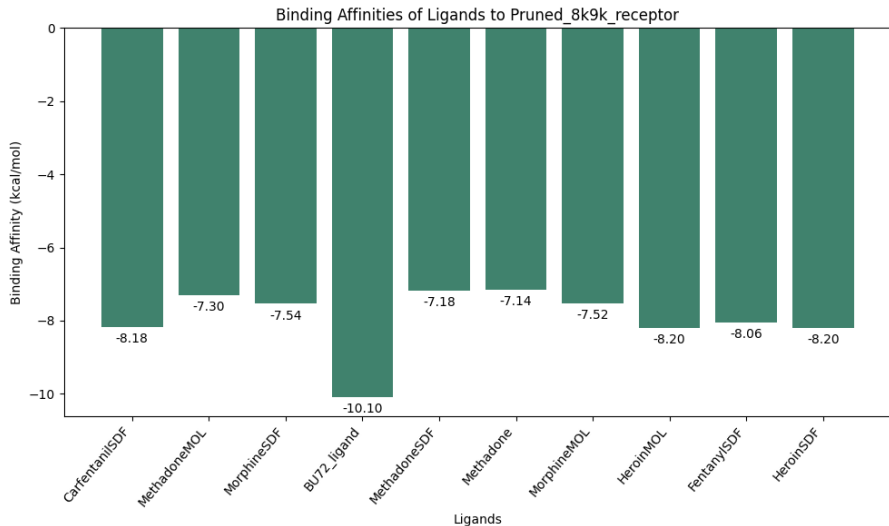


# Affinity Graphs



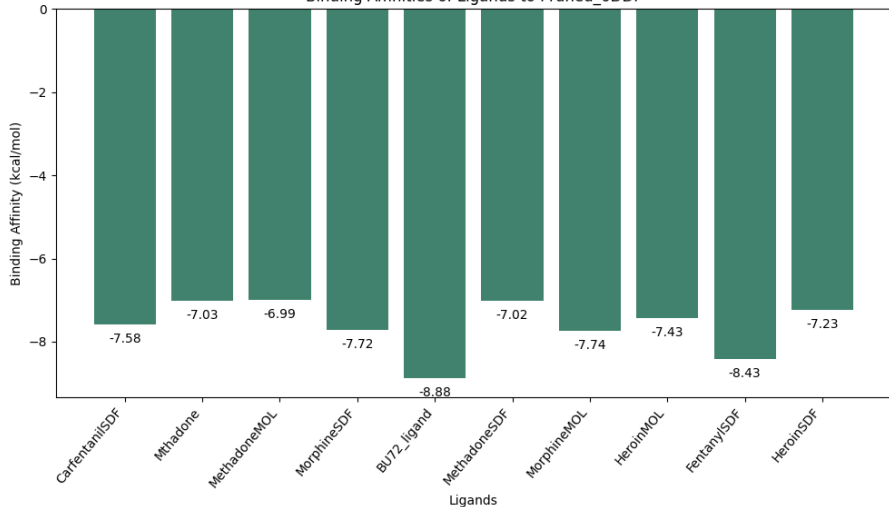


# Affinity Graphs



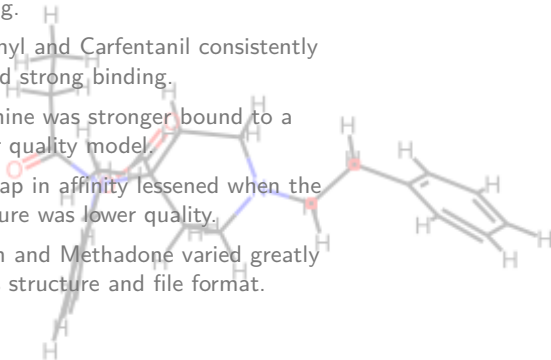
# Affinity Graphs

Binding Affinities of Ligands to Pruned\_6DDF



# 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!

