

# Protein Ligand Docking Worksheet

## Warm-Up Questions:

Read the article [“A systematic analysis of atomic protein-ligand interactions in the PDB”](#) and answer the following questions.

- 1) What are 7 of the most frequent protein-ligand interactions?
- 2) What is the most frequent protein family found in the protein data bank?

## Question #1:

List one error that you identified to be a problem prior to running the Protein Preparation Workflow.

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## Question #2:

Preparing a ligand using LigPrep may produce multiple output structures for each input structure by generating different protonation states, stereochemical outcomes, tautomers, and ring conformations. Why is it important to prepare a ligand before proceeding with docking?

## Question #3:

Why is it necessary to generate a receptor grid? What would happen if you proceeded with docking a ligand without a receptor grid?

## Question #4:

What important protein-ligand interactions do you see when the cognate ligand is docked? Take a screenshot of the Ligand Interaction Diagram below. List specific residues and define specific interactions that may play an important role in binding.

## Individual Exercise:

### Part A:

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Perform the same preparation steps on the 2XIR crystal structure. What were some of the issues with this PDB structure from the first step of protein preparation?

**Part B:**

Search the Protein Data Bank for another protein-ligand complex and do the following:

- a) Import the .pdb file into Maestro
- b) Split the structure into Ligands, Waters, and Receptor
- c) Prepare the protein using the Protein Preparation Workflow
- d) Prepare the ligand using LigPrep
- e) Detect the binding site using Receptor Grid Generation
- f) Dock all the conformations and tautomers generated from LigPrep back into the prepared protein using Schrödinger's Glide
- g) Take a screenshot of your docking results including the docking score and pose of the best docking pose.