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.
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:
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.