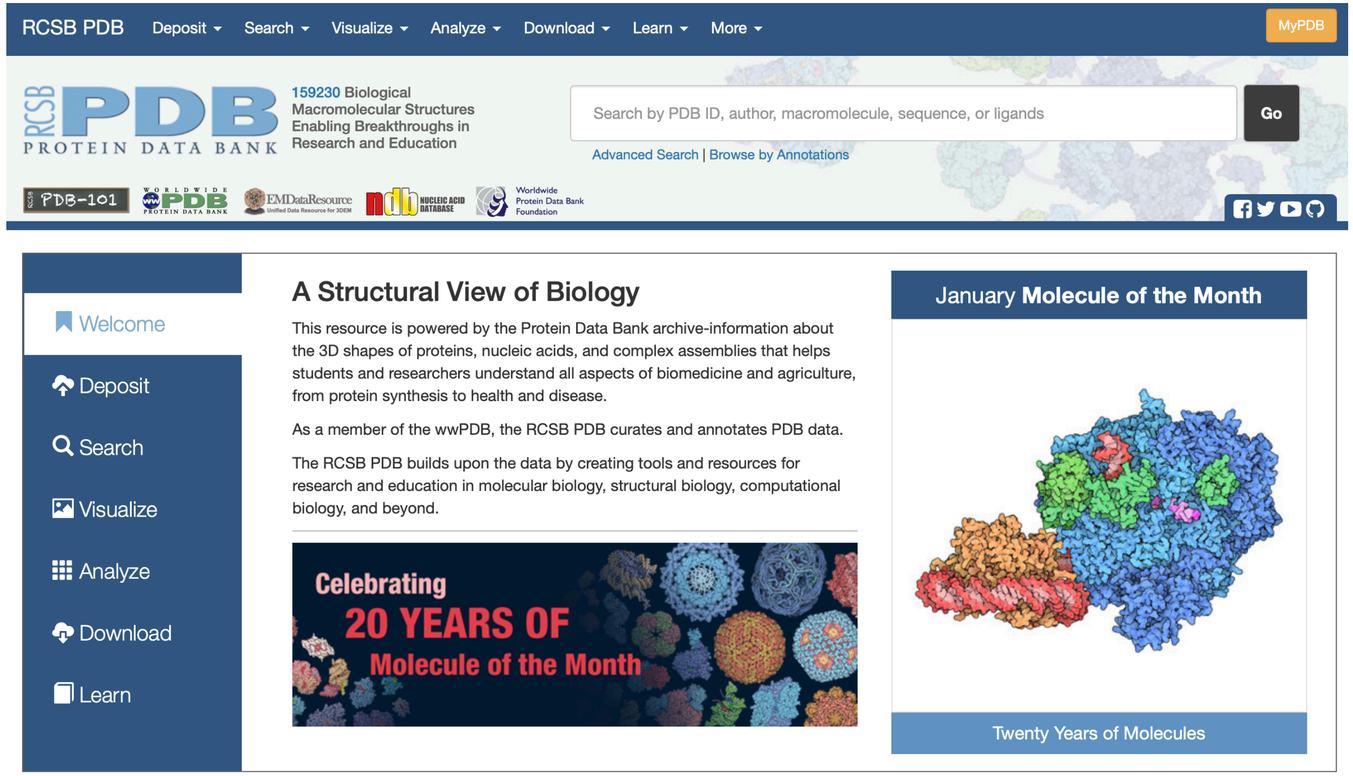
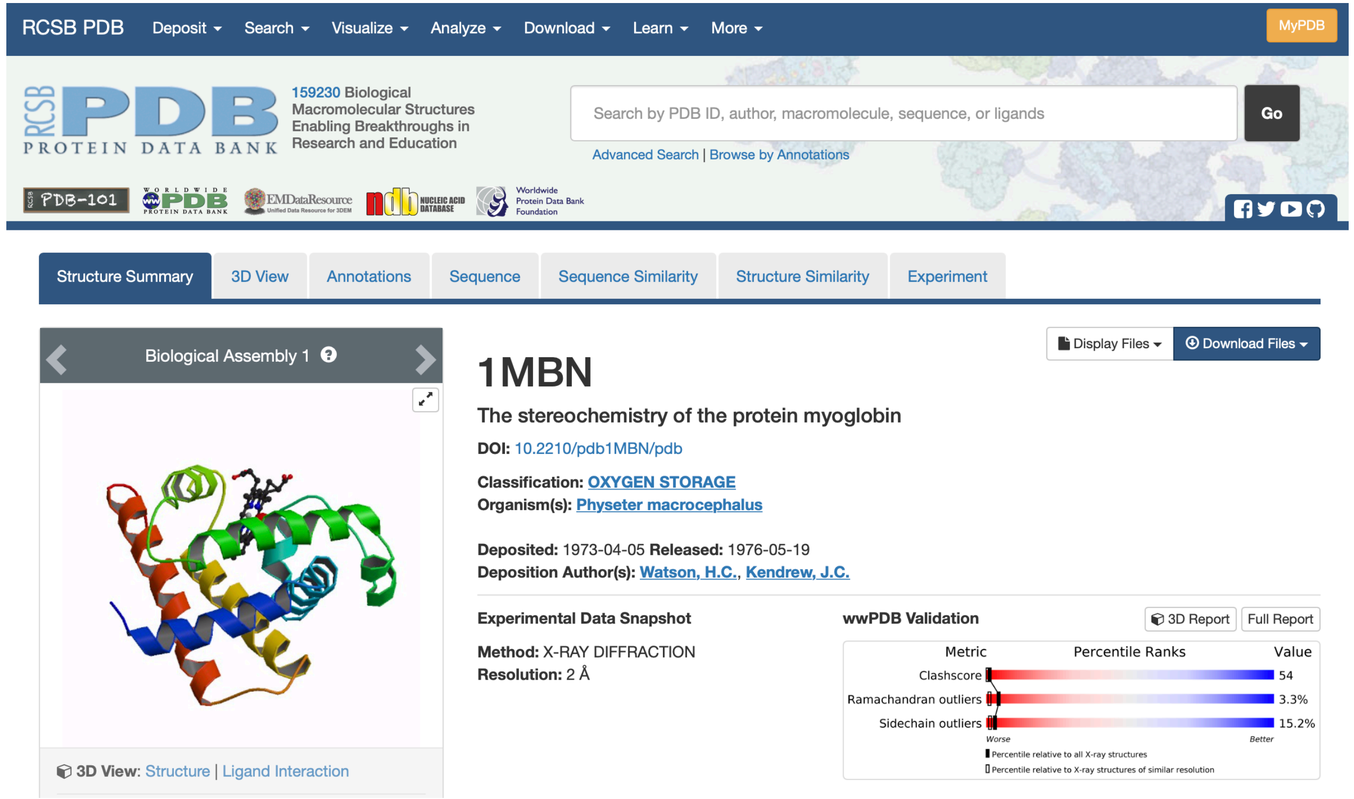
1/14/2020 Week 1 Module 1 Interactive Exercise: Visualizing Structures of Biological Macromolecules

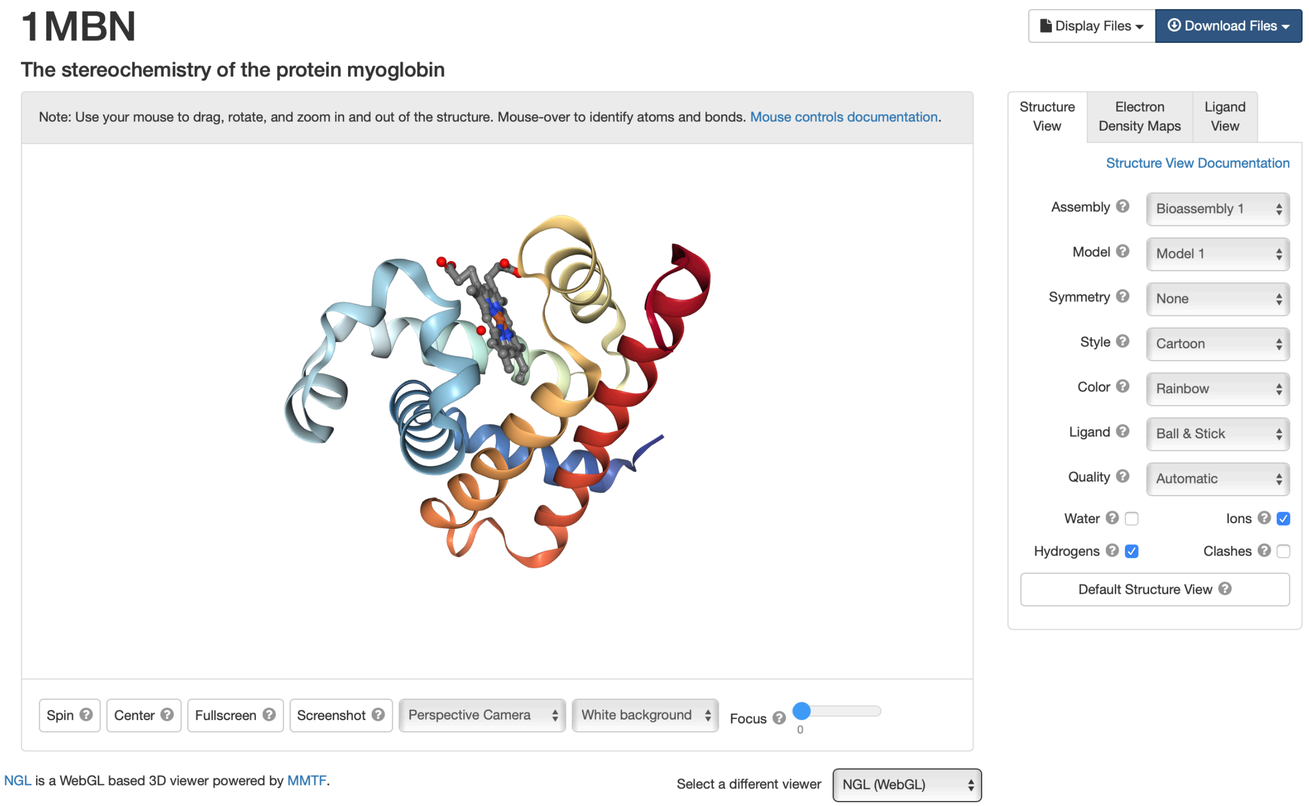
- Let's get a better feel for the structure of biological macromolecules and protein-ligand interactions by using an online visualization tool!
- Browse to the Protein Data Bank (PDB) at https://www.rcsb.org. The PDB is a public repository of experimentally determined biological macromolecular structures.



- Search for 1MBN and press “Go”. This opens the entry entitled “The stereochemistry of the protein myoglobin”. Myoglobin was the first protein structure <u>ever</u> solved.
- The page provides a lot of information about the structure, including when it was deposited into the database, how the structure was determined, and what small molecules are present in the structure. It will often provide a citation to a scientific article with more detail.

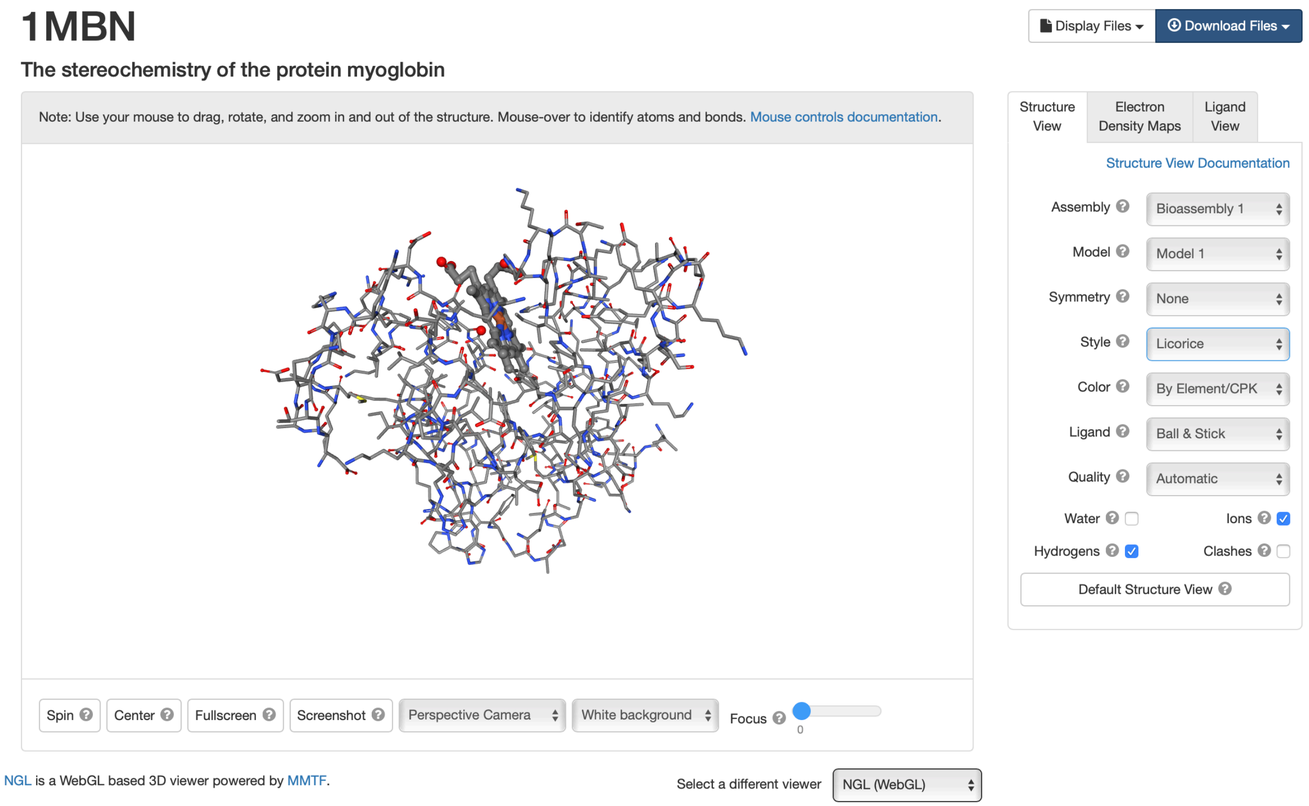


- Click on the “3D View” tab. This should open the structure using the program NGL.
- NGL allows you to interactively move the molecule and change its representation. Try rotating the molecule and zooming in and out.
- By default the protein is in a “Cartoon” style and colored by “Rainbow”. I will describe the advantages of this representation a bit later.

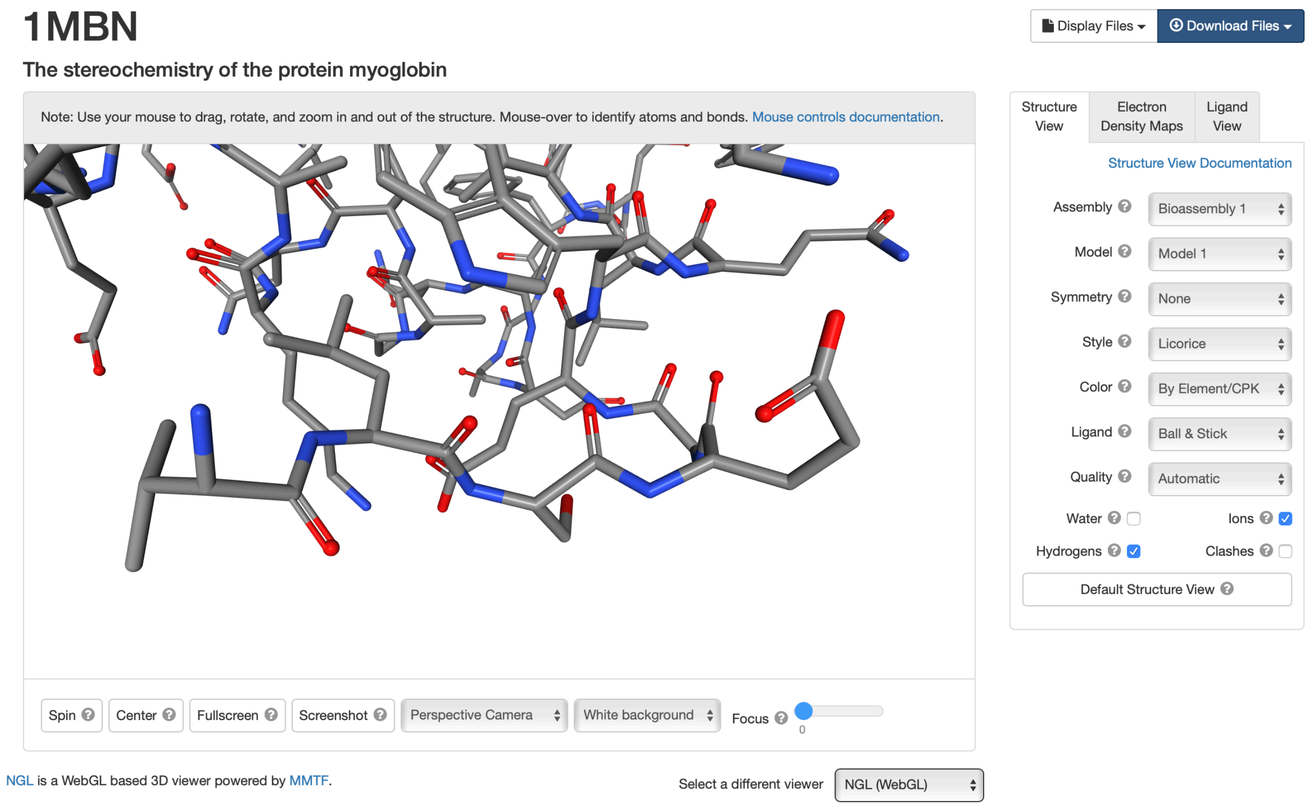


Rainbow - blue is the N-terminus and red is the C-terminus

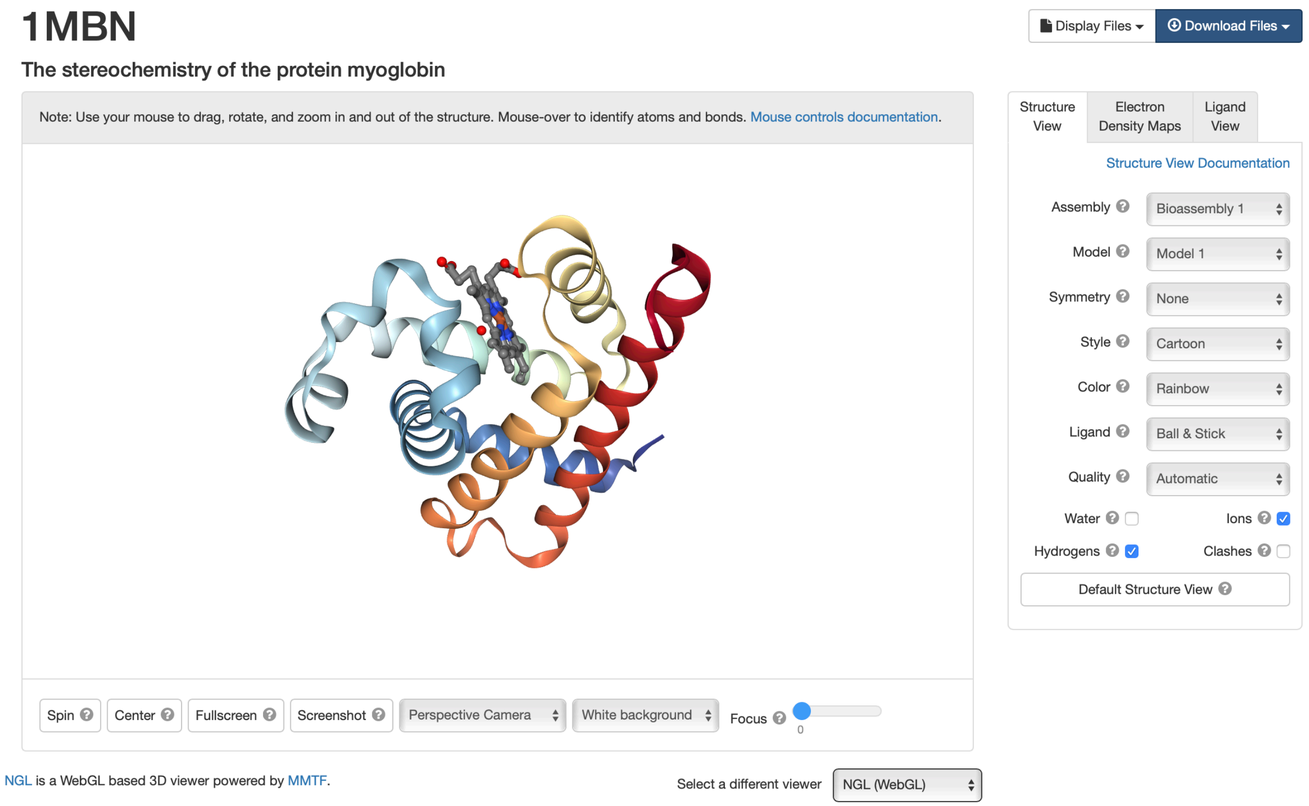
- Change Style to “Licorice” and the Color to “By Element/CPK”.
  - This representation shows <u>every single</u> covalent bond.
  - Half of each stick of licorice is colored by atom type
  - The position of hydrogen is usually not observed in structures solved by X-ray crystallography
- This representation shows where every atom is, but it is also very messy



- If you zoom into the side of the molecule, you can see that it is a branched heteropolymer with a
  - repeating backbone
  - side chains

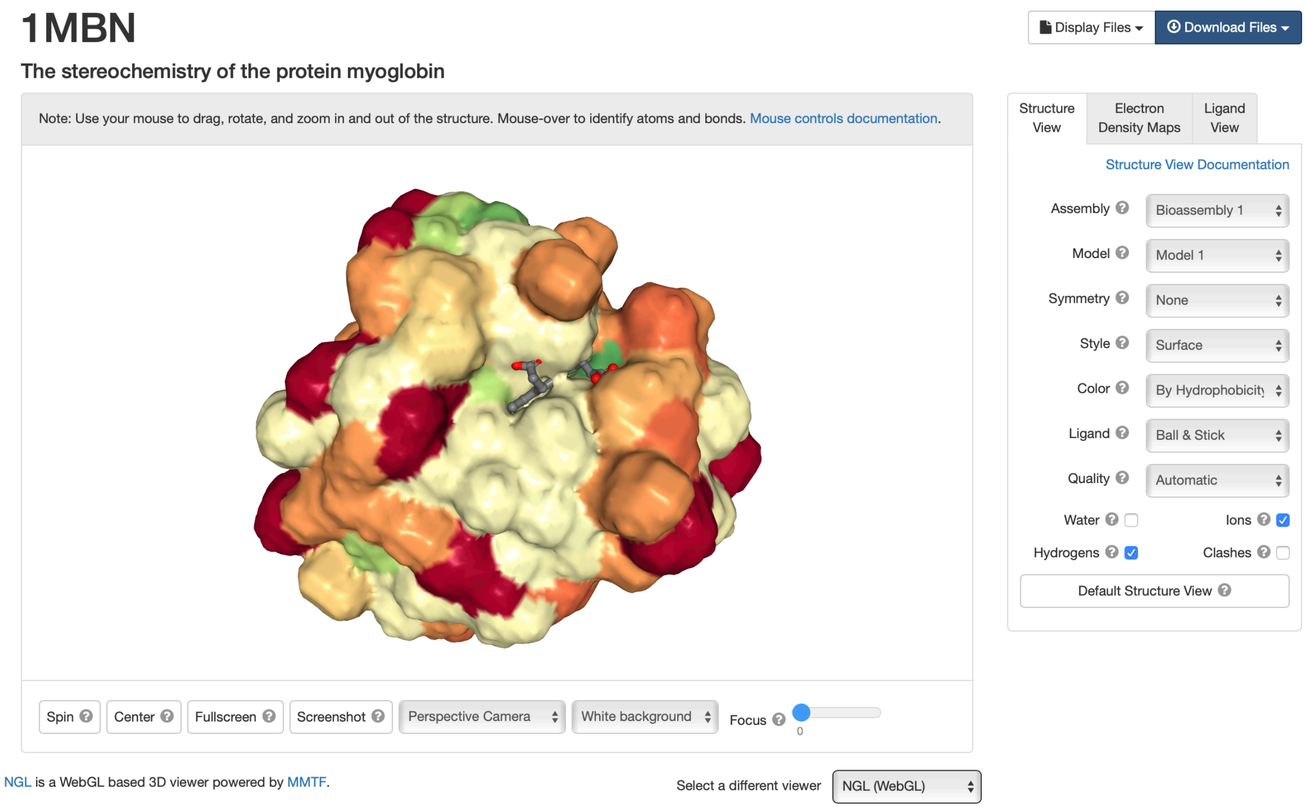


- If you go back to the “Cartoon” style and “Rainbow” color, you can more clearly see
  - the order in which parts of the protein are connected.
  - the <u>secondary structure</u>, which describes the local shape of the backbone. Myoglobin is mostly made of α helices, one of the most common secondary structure elements.
  - the <u>tertiary structure</u>, which shows the overall shape



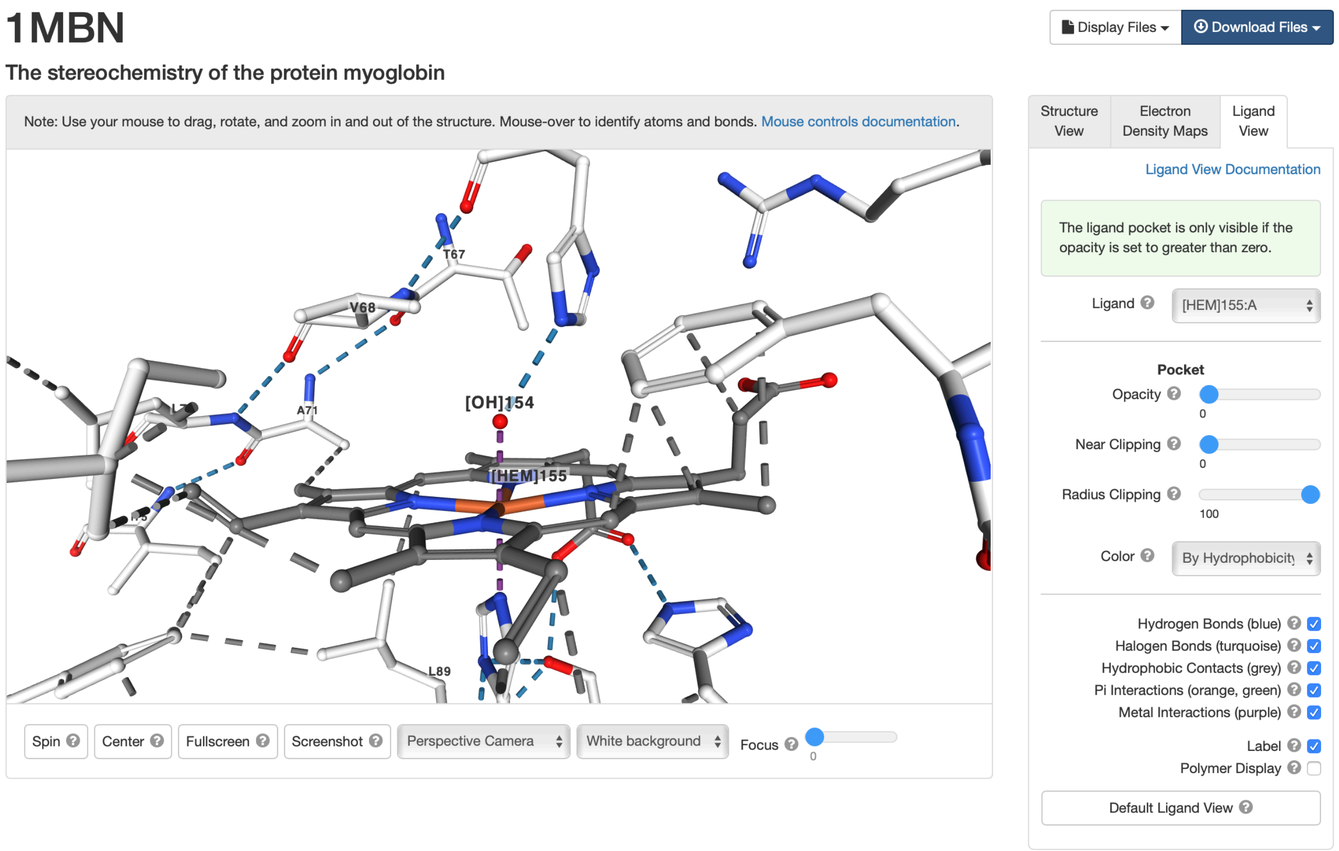
Rainbow - blue is the N-terminus and red is the C-terminus

- Change the Style to “Surface” and Color to “By Hydrophobicity”
- While “Cartoon” shows the skeleton of the protein, it can give a misleading impression about how much empty space there is. The Surface shows what the protein looks like from the outside.
- “By Hydrophobicity” will color amino acids by how much they like water.

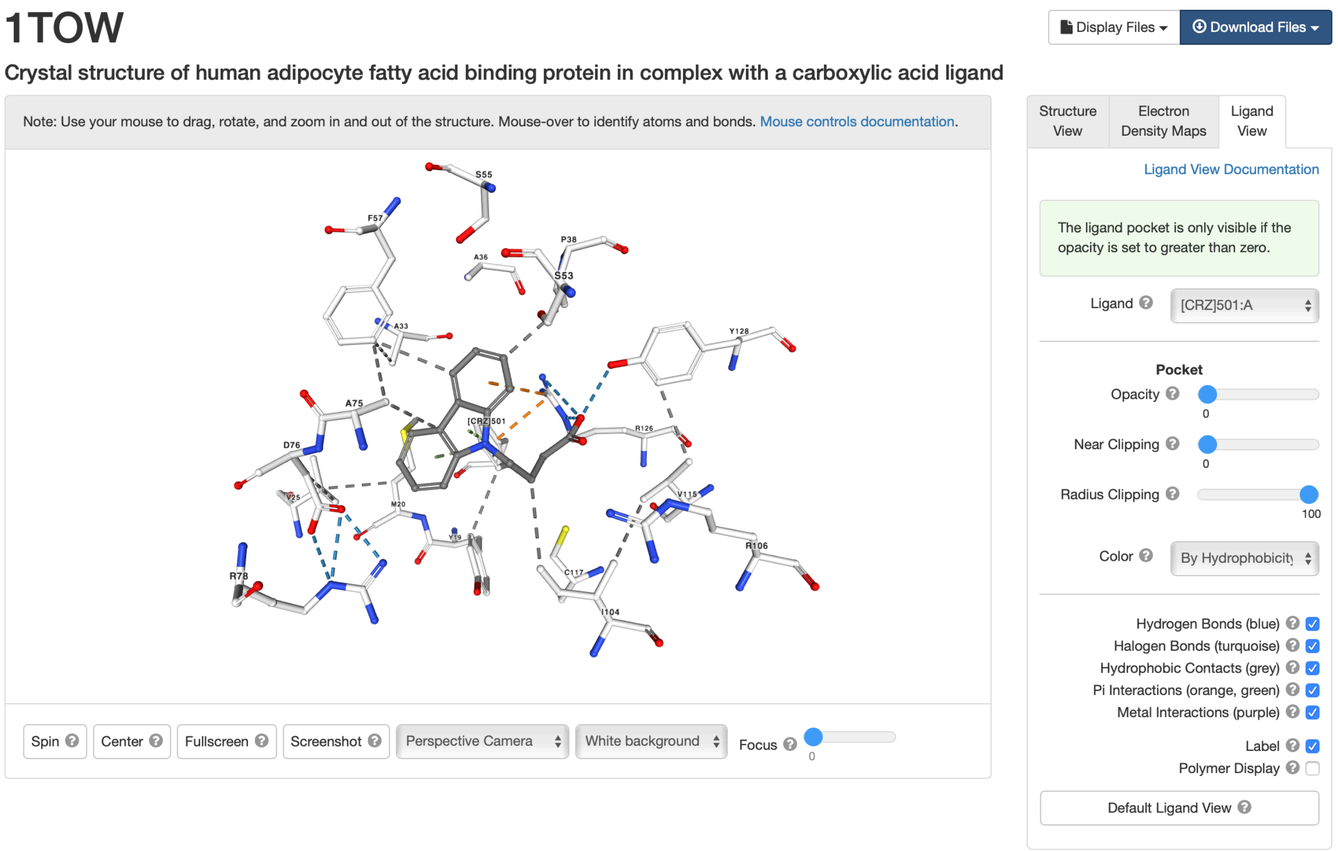
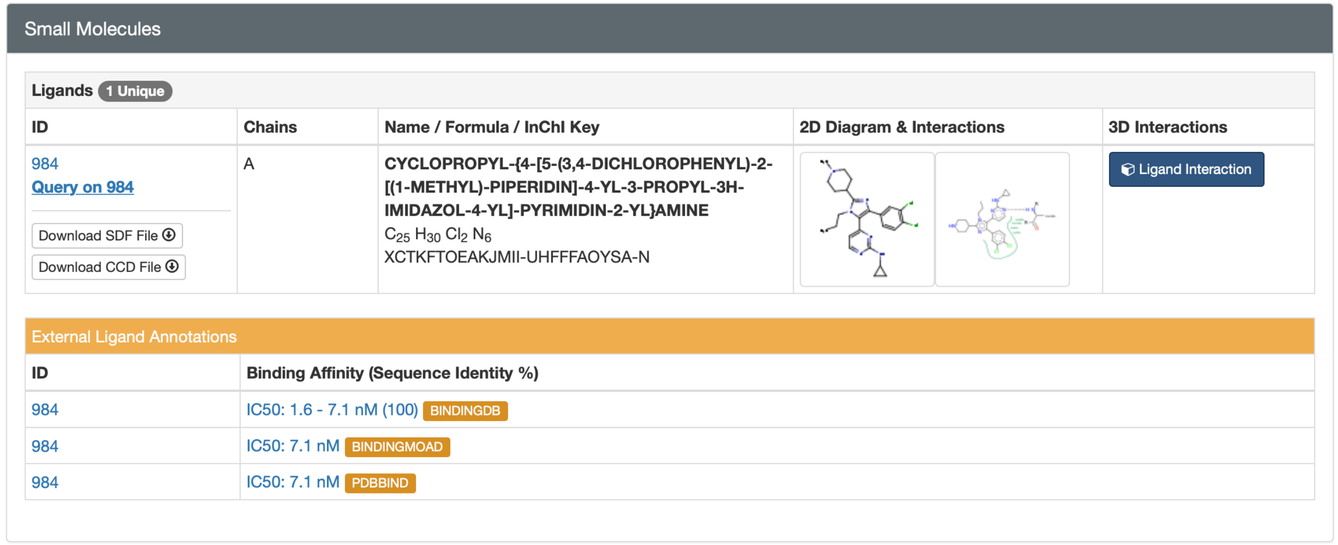
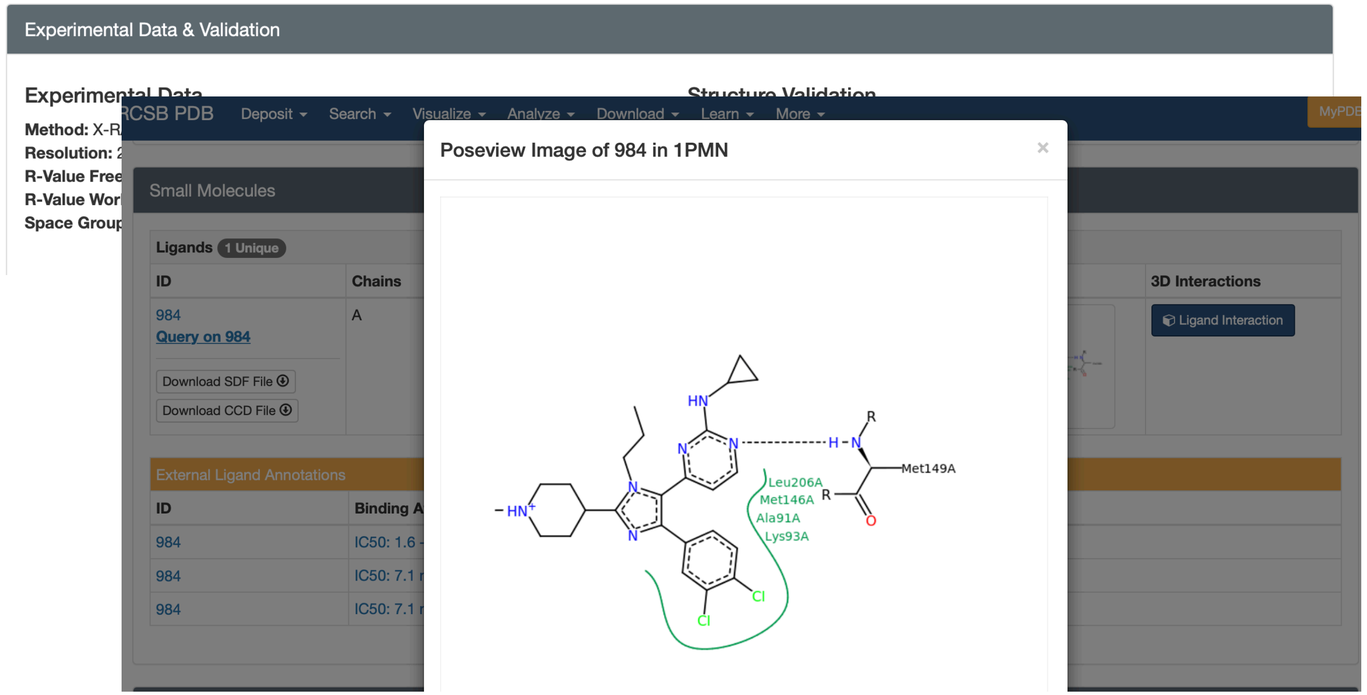


By Hydrophobicity -- colored from red (hydrophilic) to green (hydrophobic).

- Now try “Ligand View”, select [HEM]155:A as the ligand, and zoom in
- This is not a drug, but a heme prosthetic group that is noncovalently bound to the polypeptide
- Uncheck and check the types of bonds/contacts to see how they connect the heme group to the protein (these are predictions)



- For more drug-like interactions, see the ligand view for
  - PDB ID 1TOW and Ligand [CRZ]501:A
  - PDB ID 1PMN and Ligand [984]501:A



- A 3D Ligand View can sometimes look messy.
- Under the “Structure Summary” for a PDB entry, scroll down to “Small Molecules” and click on the right panel of “2D Diagram & Interactions”. This creates a Poseview Image, which more clearly shows which parts of the ligand interact with which amino acids in the protein.