Exercise 20

This exercise is to help you become more familiar with using ChimeraX to explore protein structures. You should have already downloaded this program onto your computer along with the example structure of a C. elegans glutamate gated chloride channel in complex with both its normal ligand (glutamate), it's ion that it transfers across the membrane (chloride), and a drug compound that forces the channel into an open configuration (ivermectin). Ivermectin is a powerful drug to kill worms and insects, as they, unlike humans and mammals, all utilize glutamate gated chloride channels in their nerve and muscle cells to control movement. The structure should help you understand the mechanisms of action of ivermectin.

Load the 3RIF.pdb into chimera.

1. First, let us change the default color and display features to make it a bit easier to understand the protein.
    a. Convert all of the protein chains to ribbons and hide the atomic view of the residues.
    b. Color all of the antibody chains (heavy and light) blue
    c. Color all of the glutamate gated chloride chains green
    d. Color all of the ligands red, hide the ribbon structure and show these as ball and stick atoms
    e. Change the color of the ivermectin molecules to yellow and make sure you identify all of these in the structure
    f. Change the color of the glutamate ligands to orange and make sure you can identify all of these in the structure.
    g. Make sure you can identify the chloride ion in the structure
2. Now it is useful to identify protein residues that are responsible for binding to the various ligands (e.g. glutamate, ivermectin, and chloride). These residues should be evolutionary conserved and can help you understand MSA between various glutamate gated chloride channels. Additionally, these help you understand the mechanism of action and how resistance to ivermectin could arise (e.g. the amino acids that bind to ivermectin might be mutated).
    a. For two of the ivermectin molecules, identify 6 residues that are closest to the molecule. Color these purple and also show the side chain of these. What are the types of amino acids that bind to ivermectin and what are some properties of these amino acids (e.g. polar, hydrophobic)
    b. Do the same for glutamate
    c. Do the same for the chloride ion
3. Finally, it is possible to perform many of these commands that change the color and display using the command lines. Create a text file containing all of the commands that are necessary to perform the 1st part of the problem. Verify that you can load this command file into chimera to change the color/display.