Final Project

The goal of this project is to analyze the 3D crystal structure of 3 G-protein coupled receptors (**GPCRs**). **GPCRs** are the largest and most diverse group of membrane receptors in eukaryotes. These cell surface receptors act like an inbox for messages in the form of light energy, peptides, lipids, sugars, and proteins. Such messages inform cells about the presence or absence of life-sustaining light or nutrients in their environment, or they convey information sent by other cells.

Recent advances in creating and solving protein crystal structures on transmembrane proteins has resulted in the solving of a large number of GPCR structures. In this project, we will focus on three structures: 2RH1, the β2-adrenergic receptor bound to the antagonist carazolol (a beta blocker used to treat heart arrhythmias), 4LD0, the β2-adrenergic receptor bound to the agonist adrenaline (its natural ligand), and 2YC2, the β1-adrenergic receptor bound to the antagonist carazolol. I have uploaded modified versions of these three pdb files onto t-square called B2R_Inactive.pdb (carazolol inactivates the receptor), B2R_Active.pdb (adrenaline activates the receptor), and B1R_Inactive.pdb (crazolol inactivates the receptor). In each of these pdbs, the ligand has been renamed LIG. β2-adrenergic receptor and β1-adrenergic receptor are paralogs.

Comparison of the first two structures will allow us to understand how the protein changes when it is activated by adrenaline. Comparison of the 1st and 3rd structure will allow us to understand how the physical structure is conserved across million of years of evolution.

I have uploaded two template files that contain the main code along with a file to create a class you will need for this project. You should rename the main code as **Project3_yourlastname.py** and the helper class as **HelperClass.py**. In this project, you will need to:

A. Follow the template code to take in the following positional arguments: <Inactive β2 receptor> <Active β2 receptor> <Inactive β1 receptor>
B. Send these files to a class to open these files using the appropriate methods from BioPython.
C. Perform a structural alignment on the 2nd and 3rd pdb structure to align them to the Inactive β2 receptor as a reference.
D. Create a graph to plot the number of angstroms between the residues in the inactive and active β2 receptors and the inactive β2 and β1 receptors.
E. Create a Chimera command file that changes the color of all the residues in the inactive β2 receptor that shift more than 5 angstroms to red.
F. Identify the residues in the β2 receptor that comes within 4 angstroms of the ligand. For each residue, output the position, the amino acid, and the minimum distance away from the ligand.
G. Create a Chimera command file that colors these residues in the Inactive β2 receptor green.

For this assignment you MUST follow the suggestions in the template. I.e. use argparse, use the class and functions that I created for you in the template files.