Assignment 2 Challenge Problem Setup

The challenge problem for assignment 2 involves using two software packages, PyMOL and PyRosetta 4. However, since this is a challenge problem, the TAs have limited time to help with set-up debugging. As a result, we **strongly recommend** using the LTS Macs which have all the necessary software pre-installed (see **LTS Workflow**).

First, **download and unzip the challenge problem** from the course website: http://web.stanford.edu/class/cs279/index.html#hw.

- **If you are using the LTS non-multimedia Macs**, all necessary software has already been installed. Proceed to the **LTS Workflow**. Make sure to also read the Working with PyRosetta and PyMol on the LTS machines instructions.

- **If you are running MacOS or Linux and are comfortable installing anaconda, PyMOL, and PyRosetta onto your personal computer** you should proceed with the **MacOS/Linux/WSL Local Workflow**. Make sure to also read the Working with PyRosetta and PyMol on your local machine instructions.

- **We strongly recommend** that Windows users work on the LTS machines, as PyRosetta does not run directly on Windows. If you have significant experience using the command-line interface and working in a Linux environment, we suggest that you look into Windows Subsystem for Linux (WSL), which will let you run a Linux system on your Windows machine. After installing WSL, you can follow the steps for the **MacOS/Linux/WSL Local Workflow** inside WSL. However, please note that you will need to spend a significant amount of time for installation and environment setup.

LTS Workflow

The LTS Macs have all the necessary software packages already installed. If you'd like to review instructions for connecting and using the LTS machines, visit the [Working Remotely on LTS Machines](#) document. To get started with PyRosetta, you must do this every time you log on to one of the LTS machines:

Open up terminal, navigate to your assignment 2 folder, and source the PyRosetta environment script as follows:

```
$ cd Downloads/assn2_challengeproblem/
$ source /Applications/PyRosetta/SetPyRosettaEnvironment.sh
```

Note: your assignment directory may not necessarily be in the Downloads folder.

You should get the following output:

```
Setting PyRosetta root as: /Applications/PyRosetta
Aliasing PyRosetta Toolkit GUI to pyrosetta_toolkit
/Profiles/<your suid>
```

This command sets necessary environment variables for python to access PyRosetta. You must do this *every time* you open up a new terminal window or tab.

Working with PyRosetta and PyMOL on the LTS machines

After you have implemented the required methods in the MonteCarloPredictor in assignment 2, open PyMOL. **Using the PyMOL GUI terminal**, navigate to the assignment directory (using the `cd` command), and run the following:

```
PyMOL> run PyMOLRosettaServer.py
```

You can now run predict.py (using the commands below) and observe the structure prediction in real-time from your PyMOL window:

```
$ cd Downloads/assn2_challengeproblem # navigate to your a2 dir

# After running the command below, you should see the protein change conformation
in Pymol
# Your pdb files should now be in your out directory
$ python3.9 predict.py pdbs/1prb_seq.pdb dihedral100k.pdb -dihedral -pymol -100000
```

MacOS/Linux/WSL Local Workflow

If you have not already downloaded and installed PyMOL and Anaconda, please do so now (see [Software Handout](#) from the course website).

We will now install PyRosetta 4 (watch out for the naming: PyRosetta 4 is for python 3, PyRosetta 3 is for python 2).

Installing PyRosetta

Note: You only need to follow these steps if you are working on your local computer.

1. [Download](#) PyRosetta wheel
   a. This requires getting a license:
      Go to Home - Licensing PyRosetta on the top right. Click on the 'HERE' link to purchase a PyRosetta license. The license should be free.
   b. Navigate back to the PyRosetta Downloads page. Scroll down to "Latest PyRosetta Versions, Python and Python-wheel Packages" and access the US West coast mirror.
   c. Go to the directory that fits your specific Python version and operating system. Assuming that you are using Python 3.9, this will be:
      i. For Mac: PyRosetta4.Release.python39.mac.wheel (or m1.wheel)
      ii. For Linux/WSL: PyRosetta4.Release.python39.linux.wheel
   d. Clicking on "latest.html" will automatically download the latest version.

2. Install PyRosetta 4. **Note:** if `pip install <filename>.whl` errors, try replacing `pip` with `pip3`.
   * replace <download_path> and <filename> as appropriate.
   * on line 3, replace "cs279" with your conda environment name.
   ```
   cd ~
   cp <download_path>/<filename>.whl .
   conda activate cs279
   pip install <filename>.whl
   ```

3. Confirm that PyRosetta works by running the following lines.
   First open Python by typing `python`.
   Once inside Python, try:
   ```
   import pyrosetta
   pyrosetta.init()
   ```

4. If you don't get an error with the above command, the installation was successful.

Working with PyRosetta and PyMOL on your local machine

After you have implemented the required methods in the MonteCarloPredictor in assignment 2, open PyMOL. **Using the PyMOL GUI terminal**, navigate to the assignment directory (using the `cd` command), and run the following:

```
PyMOL> run PyMOLRosettaServer.py
```

In a separate terminal window run:

```
$ conda activate <your_cs279_environment>
```

You can now run predict.py (using the commands below) and observe the structure prediction in real-time from your PyMOL window:

```
$ cd ~/assn2_challengeproblem # navigate to your a2 dir

# After running the command below, you should see the protein change conformation
in PyMOL
# Your pdb files should now be in your out directory
$ python3.9 predict.py pdbs/1prb_seq.pdb dihedral100k.pdb -dihedral -pymol -100000
```