Assignment 1 – Protein Structure and Visualization

BIOE/BIOMEDIN/BIOPHYS/CME/CS 279

Due: October 18, 2016 at 3:00 PM

The goal of this assignment is to familiarize yourself with the visualization software PyMOL and the basics of protein structure.

Acknowledgements: Portions of this assignment are based off of the PyRosetta Tutorials.

1 Preliminaries

- Download `assn1.zip` from the course website.
- Download and install PyMOL (`https://www.pymol.org/`) on your computer. If you cannot get PyMOL to run on your computer, please contact the TAs.

2 Visualizing Proteins

To start, we'll use the program PyMOL to visualize the molecular structure of some peptides and folded proteins. First, unzip the contents of `assn1.zip`, then open PyMOL. PyMOL allows you to execute instructions through their GUI or through their built-in command line.

First, in the command line, change to the assignment directory.

```
PyMOL> cd <path to assignment directory>/pdbs
PyMOL> load hras.pdb
```

When you load a structure, the default visualization is an all-atom depiction. While there are times when this is necessary/helpful, frequently, we want a coarser view of the protein. In particular, the `cartoon` view allows us to quickly learn about the secondary structures that are present in the folded 3D conformation.

To access this mode, we will hide the current depiction and then show the cartoon depiction. These commands are available through the GUI buttons in the right-most panel. In the row of the molecule we wish to manipulate (in this case `hras`), select the following commands.

`H` → `everything` `S` → `cartoon`

If you prefer, you can also control the depiction from the command line.

```
PyMOL> hide everything, hras
PyMOL> show cartoon, hras
```

In this visual mode, alpha helices are depicted by twisting coils and beta strands are depicted as fat arrows.

Question 1:

(a) How many sections of hras are folded as an alpha helix?

(b) How many strands of hras are folded as a beta strand?

Note: You may find it useful to color by secondary structure.

C → by ss → Helix Sheet Loop

2.1 Backbone Geometry

Next, we will take a closer look at the typical secondary structures, the alpha helix and beta sheets. Start by reinitializing PyMOL and then running the following commands.

```
PyMOL> reinit
PyMOL> load helix.pdb
PyMOL> hide everything
PyMOL> show cartoon
```

Question 2: *Looking down the helix and moving away from the viewer, which direction is the helix coiled (clockwise or counterclockwise)?*

The geometry of an alpha helix (and a beta strand) refers to a specific orientation of the atoms in the polypeptide backbone. In general, the orientation of the backbone atoms tells us a lot about the overall structure of the protein. To select just the backbone atoms, execute the following commands.

```
PyMOL> hide everything
PyMOL> select bb, name c+o+n+ca
PyMOL> show lines, bb
```

You should see the backbone atoms represented as connected lines, with carbons in green, oxygens in red, and nitrogens in blue.

The backbone geometry can be succinctly described by the *dihedral angles* (also known as torsional angles). In general, a dihedral angle is an angle between two planes. In the context of backbone molecular geometry, we are concerned with the angle between atoms while "looking down" a bond.

Question 3: *We will be looking at residue 159. Which amino acid does this correspond to?*

(a) Compute the dihedral angle ϕ_{159} *(between* $C_{i-1} - N_i - C_i^\alpha - C_i$*).*

(b) Compute the dihedral angle ψ_{159} *(between* $N_i - C_i^\alpha - C_i - N_{i+1}$*).*

(c) Compute the dihedral angle ω_{159} *(between* $C_i^\alpha - C_i - N_{i+1} - C_{i+1}^\alpha$*).*

Select the atoms in the correct order, and then use the following command to compute the appropriate dihedral angles.

```
PyMOL> get_dihedral (pk1),(pk2),(pk3),(pk4)
```

Note: Use the `pkAt` *command (by default double-clicking with the right click).*

Due to the chemistry of the peptide bond between $C_n - C_{n+1}$, ω is generally very close to 180° (and rarely, 0°). Next, perform the same computations for the beta sheet segment (contained in `pdbs/bstrand.pdb`).

Question 4: *Are the beta-strands running parallel or antiparallel to one another?*

Question 5:

(a) Compute ϕ_{41}*.*

(b) Compute ψ_{41}*.*

(c) Compute ω_{41}*.*

Now that we have computed the dihedral angles for two amino acid residues, it is natural to ask whether these measurements are typical. In fact, one way of characterizing proteins' secondary structures is by their ϕ and ψ angles.

In particular, one way to represent the distribution of backbone dihedral angles is a Ramachandran plot. Ramachandran plots are two-dimensional heat maps, which represent the number of residues present for a given ϕ and ψ.

Question 6: *Generate a Ramachandran plot for the alpha helices (saved in* `helices.pdb`*), the beta strands (saved in* `bstrands.pdb`*), and full hras protein. Use the STAN server to generate the plots (*`http://xray.bmc.uu.se/cgi-bin/gerard/rama_server.pl`*). Identify the regions in the plot for hras that correspond to alpha helices and beta strands.*

2.2 Hydrogen Bonds

A *hydrogen bond* is an attractive force between molecular dipoles involving hydrogen. While the hydrogen atoms are not drawn in the backbone (because they were not resolved in the experimental

structure), there is a partially positive hydrogen bonded to (almost) every nitrogen involved in the peptide backbone, which tends to be attracted to the partially negative oxygens in the backbone. To visualize these "bonds", we can measure the lengths between groups of atoms, specifically where polar contacts occur. First, we will add hydrogens into the structure in PyMOL and then show the backbone H-bond distances. Reinitialize PyMOL, and load helix.pdb from the pdbs subdirectory in the assn1 folder. You should hide everything, then enter the following commands.

```
PyMOL> select bb, name c+o+n+ca
PyMOL> show lines, bb
PyMOL> h_add
PyMOL> distance hbonds, name o, name n, mode=2
```

Note: `mode=2` selects polar contact distances.

Question 7: *For this question, please use **helix.pdb**. What is the average length of H-bonds in this alpha helix? What is the **integer** offset between residues that are interacting (ie if two residues share a H-bond in an alpha helix, what is their positions in the protein backbone relative to each other)?*

Question 8: *Next use **bstrand.pdb**. What is the average length of H-bonds between these two beta-strands? Does the average H-bond length differ significantly if the strands are parallel or anti-parallel (hint: use the bstrands.pdb)?*

3 Feedback

You will receive full-credit for this portion for providing any response. We encourage constructive criticism.

Question 9: *What was your favorite aspect of the assignment? What was your least favorite aspect of the assignment? Why? Any suggestions for improvement?*

Question 10: *Approximately how long did this assignment take you? Where did you spend most of this time?*

4 Submission Instructions

Upload your writeup, which you should name `writeup1.pdf`, to `corn`. If you want to handwrite your writeup, this is fine, just scan it as a pdf and verify that it is legible. Then, change to the directory containing `writeup1.pdf` and enter the following command.

```
/afs/ir/class/cs279/scripts/submit.py assn1 .
```

You should see a message indicating a successful submission. If you have any issues submitting, let us know! You may resubmit if you discover things you would like to change in your work.