Assignment 1 – Protein Structure and Visualization

BIOMEDIN/BIOPHYS/CME/CS 279

Due: October 8, 2015 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 or copy it into your AFS space (see Accessing Software)
- Obtain access to PyMOL and PyRosetta (see Assignment 1 Setup)

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 assn0.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>/psp
PyMOL> load pdbs/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> load pdbs/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:

(a) Compute the dihedral angle $\phi_{157}$ (between $C_{156} - N_{157} - C_{\alpha_{157}} - C_{157}$).

(b) Compute the dihedral angle $\psi_{157}$ (between $N_{157} - C_{\alpha_{157}} - C_{157} - N_{158}$).

(c) Compute the dihedral angle $\omega_{157}$ (between $C_{\alpha_{157}} - C_{157} - N_{158} - C_{\alpha_{158}}$).

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

```
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 $C_n - C_{n+1}$, $\omega$ is generally very close to 180° (and rarely, 0°). Next, perform the same computations for the beta sheet segment (contained in `pdb/bstrand.pdb`).

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

Question 5:

(a) Compute $\phi_{51}$.

(b) Compute $\psi_{51}$.

(c) Compute $\omega_{51}$.

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 $\phi$ and $\psi$ 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 $\phi$ and $\psi$.

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 using script `ramaPlot.py` from the terminal. Please ignore the warning about the missing atom on the C-terminus and be sure to load the PyRosetta module prior to running the python script.

```
python ramaPlot.py <file1>.pdb [<file2>.pdb ...
```

Identify the region in the plot for hras that corresponds to alpha helices and which corresponds to 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. 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**: What is the typical length of H-bonds in the 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**: What is the typical length of H-bonds in the beta sheets?

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.