

## **BIOC 565 PROBLEM SET 1: Due September 5**

**Questions 1-3 have you use your newfound DeepView fluency to analyze the structure of lysozyme (1HEW.pdb)**

### **HYDROGEN BOND INTERACTIONS**

*Set the Deep View parameters for detecting hydrogen bonds as follows: Under **Preferences:H-bond detection threshold**, set the threshold detection parameters Min Dist 2.2 Å, Max Dist 3.5 Å ± 0.05, min angle 90°. Note that the distances here are between the acceptor and donor, and the minimum angle actually refers to **any** angle involving the donor, acceptor and any third atom covalently bonded to either the donor or acceptor (these third atoms are also called the donor and acceptor antecedents). These are the criteria on which Deep View judges H-bonds. Once you've set these parameters, compute and show the H-bonds as green dashed lines, as learned in the tutorial.*

**1.** In protein structures determined by crystallography, asparagine and glutamine side chains have an interesting structural ambiguity. When modelling the side chain atoms into the experimental electron density map to generate the structure model, one cannot usually distinguish between the electron density for the O<sub>δ1</sub> atom and that for the N<sub>δ2</sub> atom, since nitrogen and oxygen are nearly the same size and the hydrogens on the nitrogen are not visible. Thus, two conformations are equally compatible with the data. However, sometimes the correct orientation of the side chain amide group can be guessed from the hydrogen bond interactions it appears to make with other groups in the protein. **There are three glutamines in lysozyme. For which of them is the orientation ambiguous? For any that are not ambiguous, do they appear correctly oriented? Make drawings of any hydrogen bond networks you see, with residues labelled.**  
*Hint: The way I would do this in Deep View is to first identify the glutamine residues and then analyze them one at a time, first by displaying and centering each one and then by identifying any nearby chemical groups using the **Select:Neighbors of selected aa...** function. This function will pop up a dialog box: choose to **add to the selection any groups within 5 Å**. Then display and center the selected residues, and you'll be able to see what is nearby each glutamine.*

**2.** There is a "bug" in Deep View (at least the version on the computers in BSW 243) regarding how it treats hydrogen bonding by the side chain nitrogens in histidine and tryptophan. For example, look at the sidechain/sidechain hydrogen bonding interaction

between Asn 27 and Trp 111. Select and display these two residues, and have Deep View compute hydrogen bonds. None should appear between the side chains. Note, however, that the carbonyl oxygen of Asn 27 and the epsilon-1 nitrogen of Trp 111 appear well-positioned for a hydrogen bond. **For this donor-acceptor pair, measure and report the distances, angles and dihedral (torsional) angles suggested by Presta and Rose as criteria to use when hydrogen coordinates are not present (see the third lecture, slide #5).** These include the N...O distance, the N-O-AA, DD-N-O, and DD'-N-O angles (assignment of DD and DD' is arbitrary), and the N-DD-DD'-O torsion angle (again, assignment of DD and DD' is arbitrary). **Does the hydrogen bond geometry look basically reasonable according to these criteria?** Now, click the "Torsion" button on the toolbar and click on Asn 27 in the display. Using the lower set of arrows (black triangles) at right end of the toolbar, rotate the  $\chi_2$  angle until the side chain nitrogen is roughly where the carbonyl oxygen used to be. **What happens? What do you think the "bug" is?** Remember to use the Ctrl key in combination with the dihedral angle button on the toolbar, to be able to measure a torsion angle involve four selected atoms.

### RAMACHANDRAN PLOT

**3.** The region around (60, -120) in a Ramachandran plot, though sterically disfavored, is occasionally populated by residues (mostly glycines) involved in Type II' tight turns. A Type II' tight turn is characterized by an  $i, i+3$  main chain hydrogen bond, and (phi,psi) near (60,-120) and (-80,0) for residues  $i+1$  and  $i+2$  respectively. **Is Gly 104 of lysozyme, which has phi,psi around 60,-120, actually involved in such a Type II' turn? Draw a diagram to illustrate your answer.**

**Questions 4-7 review some of the lecture material:**

4. Based purely on considerations of chemistry, what portion of the sequence below could be spliced out as an intein? What would the product sequence be?

MLLDDIESYFGRIEKVAAF~~GIMMEAVYQWRNRPGQLIPKGRAAEAAAYRNCGRLPFKPEL~~  
YEKSNG

5. In the asparagine deamidation reaction, what is the alternative hydrolysis product of the succinimide ring, i.e. the one not pictured in the lecture notes?

6. Draw all three reasonable resonance forms for the delocalizing the positive charge on the cationic guanidinium group on the side chain of arginine. Include all hydrogens and lone pairs, and arrows showing how electrons are "pushed" to interchange the resonance forms.

7. Draw Newman projections that represent the canonical  $g-g^+$  rotamer (referring to conformations around the  $\chi_1$  and  $\chi_2$  angles, respectively) of leucine.

**For questions 8-10**, download the PDF file for the following article from the course website: Lovell SC, Davis IW, Arendall WB, de Bakker PIW, Word JW, Prisant MG, Richardson JS, Richardson DC *Proteins Struct. Funct. Gen.* **50**: 437-450 (2003). Alternatively, if you need some practice finding articles on the Web on your own, try doing a PubMed word search for the article (using the PubMed link on the Cordes section links page). Click on the author list for the PubMed entry to see the Abstract page, and then get the PDF via the Wiley Interscience icon link at the upper right hand corner of the Abstract page. This article is (in part) a survey of phi/psi angle combinations in protein structures determined at high resolution; reference is made to these results several times in the Richardson review. You don't need to read the entire Lovell article, just the parts that allow you to answer the questions below.

**8.** Look at Figure 4. Notice that proline has a very different distribution of observed phi,psi values from other residues. Explain why this should be so, in no more than a couple of sentences.

**9.** Notice also in Figure 4 that pre-Pro (coming directly to the N-terminal side of Pro) residues have an unusual set of observed phi,psi values. Draw a diagram to suggest why psi values around zero would be disfavored in pre-Pro residues.

**10.** Why do Lovell *et al.* suggest that the (-150, -60) region ("left of alpha"), while sterically permitted in hard-sphere models, is almost never observed in proteins? What argument do they rule out and why?