Biomolecular Structure Exam #1

This exam is to be worked on independently. You must not talk, or otherwise communicate, with *anyone* other than Professor Martin about *any* aspect of the exam. You may not communicate with your fellow students in the class, nor with any other colleagues, faculty or student.

Due in Craig Martin's office (LRGT 403D, October 16, 9:00am

Honesty and integrity are absolute essentials for this class. In fairness to others, dishonest behavior will be dealt with to the full extent of University regulations.

1. For the first question, examine structure 2drv from the PDB (a Jmol presentation is available for your benefit on our course WEB page) and answer the following questions:

a) Examine the interface between the two subunits. Describe the chemical nature of this interface and what forces you think drive and/or are important in subunit-subunit interactions.

(10 points) Note the number of water molecules (pink) at the interferface. This is unusual. There are some hydrophobic contacts (green), and they are certainly expected to help drive association, but not as much as at some protein-protein interfaces. Water-mediated H-bonds between amino acids on opposite sides of the interface are expected to be less precise than more direct contacts. One might expect this interface to be more "loose" than some.

b) Looking at the location of amino acids 83 to 92, do you expect this stretch to be polar, nonpolar, or amphipathic? Is your prediction upheld? Explain your prediction.

(10 points) Helix 83-92 is predicted to be (and is) amphiphilic, since it lies at the surface of the protein. Amino acids facing solvent are polar and residues facing the hydrophobic interior are nonpolar. Sequence is Ser-Leu-Tyr-Glu-Val-Leu-Glu-Ala-Ile-Lys -- the center is a mix of hydrophobic and polar.

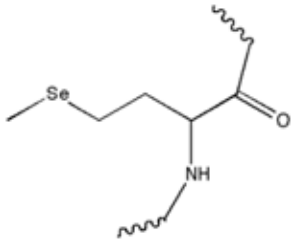
c) Looking at the location of amino acids 98 to 104, do you expect this stretch to be polar, nonpolar, or amphipathic? Is your prediction upheld? Explain your prediction.

(10 points) Strand 98-104 is buried within the protein and so is expected to be uniformly nonpolar. It is, except at the ends, which are near the protein surface. Sequence is Gln-Leu-Trp-Phe-Leu-Val-Arg -- the center is uniformly hydrophobic.

d) Briefly describe the subunit and domain structure of this protein. Justify your explanation.

(10 points) This protein is clearly composed of two subunits, chains A and B. But you can also recognize that each subunit is composed of two domains, each with an independent hydrophobic core. However, the construction is complicated in that the cores are not simply built from one contiguous chain in each.

e) This structure contains heteroatoms. Draw the chemical (structural) formula for the heteroatom MSE in this structure, using classic organic structure notation. Attach a separate sheet with your drawing of the structure.



(5 points) This is selenomethionine, incorporated as an amino acid in the protein. That it is not a separate molecule can be deduced by turning on the rest of the backbone. But also looking at the coord struct of MSE alone was a tip - it was not a complete amino acid (look at what should be the carboxylate end - it's not a carboxylate).

2. For the second question, examine structure 2r13 from the PDB (a Jmol presentation is available for your benefit on our course WEB page) and answer the following questions:

a) In the JMol presentation at our WEB site, toggle between the two surface views. Explain what you think is the difference between the two views (something more deep than "one is smoother than the other"). Explain why one view is "better" than the other.

(10 points) You might reasonably surmise that the tighter surface is using van der Waals radii, while the "fatter" view is likely something like the solvent accessible surface (indeed this is what they are). The latter more accurately reflects the surface of the protein in that we're never concerned about He and H_2 making van der Waals contact, but rather, we're interested in how larger (small) molecules and proteins interact. Some of you seemed to miss the point that these are just two different views of reality - remember, the molecule is what it is - these are just different ways for us to think about that reality.

b) Given your understanding of protein structure, explain ***why*** this molecule is unlikely to adopt this precise structure as a monomer in solution.

(15 points) The stretch from 32 to about 40 is sticking out in solution - no hydrophobic core (though some of it is hydrophobic), nothing to stabilize that structure (except likely in the crystal structure, contacts with other molecules). This is not stable in that one conformation regardless of whether the stretch were hydrophobic or hydrophilic.

3. For the third question, examine structure 2OZB from the PDB (a Jmol presentation is available for your benefit on our course WEB page) and answer the following questions:

a) Explain the role and interactions within this structure of Glu 41 of chain D.

(15 points) We can see that Glu 41 interacts with G32 via H-bonds, while simultaneously interacting with Arg 36, which contacts a DNA backbone phosphate and the 2'=OH of G43. Thus each amino acid "buttresses" the other, with the aid of the two DNA contact points - cute. Note that all of these interactions are not equivalent. Indeed, while the 3 contents made by OE1 of Glu41 are all of about the same distance, the angles are better for 2 of the 3. Can you discern the differences?

b) Explain the role and interactions within this structure of His 270 of chain E.

(15 points) His 270 stacks onto A39, stabilizing an otherwise exposed hydrophobic end of the DNA. It also makes H-bonds to the 2' hydroxyl of A39 and to a DNA backbone phosphate. Some of you noted H-bonds from His270 to A39. While the distances are acceptable, the angles are terrible. His270 can make no reasonable H-bonds to any atom in A39. Think about where the orbitals are, and then think about orbital overlap.