Chem 791B **Biomolecular Structure** **Exam #1**

Exam Due: Thursday, November 16 in class - no exceptions

This examination is open book, but is to be worked on ***independently***. Once you have begun working on the exam, you may not discuss any aspect of the exam with *anyone* other than C. Martin. This includes any discussions with anyone after you are done with the exam, but before November 16.

You are on your honor.

Note: The following questions are looking for short, concise, but complete answers. Overly long responses typically indicate a lack of thorough understanding, and will be scored accordingly. Be concise. Lay out all of your thoughts before you write your final answer. Choose only those relevant.

1) Go to the Protein 1 site on the Exam Web page.

See the WEB Site for extended answers and figures.

a) (15 points) Draw a topology diagram for this protein. What class of protein is it?

This is a fairly distorted beta barrel protein, despite the fact that Rasmol does not identify all of the beta strands (but you should recognize them). You should identify it as an antiparallel sheet protein. See WEB site for topology diagram.

b) (10 points) What interaction(s) drive folding for this protein?

As for more conventional beta barrel proteins, the sheets stack on each other with hydrophobic surfaces pointing towards the inside of the barrel. More hydrophobic chains point inwards. As discussed in class, this hydrophobic core (hydrophobic collapse) is what *drives* protein folding.

c) *Extra credit*: (5 extra points) what is unusual about this protein (at least two things)?

1) Chain numbering is screwy. 2) multiple aa side chains at 3 positions.

This is PDB entry 1G2B. From the remarks section of that file, we have:

REMARK 999 THIS IS A CIRCULAR PERMUTANT OF THE WT ALPHA-SPECTRIN
REMARK 999 SH3 SEQUENCE (PDB CODE WT-3D STRUCTURE: 1SGB). THE
REMARK 999 RESIDUE NUMBERS ARE AS IN THE WT SPECTRIN-SH3 DOMAIN
REMARK 999 (1SGB). THR 4 (N-TERMINUS) AND ASP 62 (C-TERMINUS) OF
REMARK 999 THE WT-SH3 SEQUENCE ARE LINKED BY TWO ADDITIONAL
REMARK 999 RESIDUES (SER 2, GLY 3). THE CHAIN IS CLEAVED BETWEEN
REMARK 999 ASN 47 AND ASP 48. MET 0 IS ADDED AT THE NEW N-TERMINUS.

2) Go to the Complex 2 site on the Exam Web page.

For the answers to this section, please go to the class WEB Site.

a) (10 points) Explain the stabilizing interaction(s) that Tyr 34 on chain C makes with amino acids in chain A (protein-protein interaction).

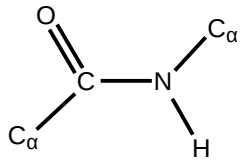
b) (10 points) Arg 74 on chain C makes sequence specific contact with the RNA. Explain the important aspects of this contact.

c) (5 points) Arg 74 on Chain C is also weakly "buttressed," to stabilize the above interaction. Explain the buttressing.

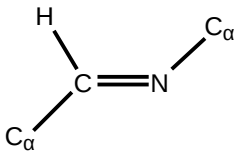
d) (5 points) Is the interaction between chain B and the RNA similar to the classic helix-turn-helix interaction that we learned about in class? Explain.

e) (5 points) Draw a "topology diagram" (2D representation) of the RNA. How many co-axially stacked helices are there? Explain

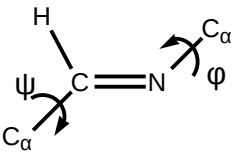
3) Assume that the protein backbone were composed of imine linkages , instead of the normal peptide linkage.



Peptide



Imine



For proteins in general, how would this change effect:

For the folding reaction: Unfolded ⇌ Folded

a) (10 points) hydrophobic standard free energy of folding ($\Delta G_{hydrophobic}$)

There might me a slight decrease in the hydrophobic standard free energy of folding. This linkage is more nonpolar than the peptide linkage (in its unprotonated form), hence the hydrophobic core of the folded state would be more hydrophobic (relative to the unfolded state).

b) (10 points) H-bonding standard free energy of folding ($\Delta G_{H\text{-}bonding}$)

This linkage will form hydrogen bonds less readily (note that deprotonation of the C-H proton is very unfavorable). However, this will effect both the folded and unfolded forms of the protein. Depending on one's perspective, this substitution will have little, or a slightly positive (destabilizing) effect on the H-bonding contribution to the free energy of folding.

c) (10 points) electrostatic standard free energy of folding ($\Delta G_{electrostatic}$)

Relatively small effect. The normal peptide bond has a distinct dipole and so could be argued to have some electrostatic interactions, both with water in the unfolded state and with other dipoles (eg., aligned in an α–helix) in the folded state. The imine linkage has a much smaller dipole and therefore will not interact electrostatically with water in the unfolded state nor with other dipoles in the folded state.

d) (5 points) configurational entropy of the folded protein (S_{config})

Little change, see below

Answers which argue that the substitution might allow a less precisely folded protein, and therefore an increase in entropy of the folded protein are acceptable. A protein based on this linkage might be more stable (hydrophobic collapse - part a), but might behave more like a lipid bilayer (less ordered).

e) (5 points) configurational entropy of the random coil (S_{config})

By definition, the folded protein has little configurational entropy associated with the backbone, regardless of linkage (assuming no unstructured domains in the "folded" protein). However, the configurational entropy of the unfolded form will *increase* in going to the imine linkage. Many noted that the imine double bond is stronger than the peptide C-N bond. However, the peptide C-N bond already has a very high barrier to rotation. A still higher barrier won't change things too much. However, the phi and psi angles will have more allowable ranges in the imine linkage (less steric repulsion with the carbonyl oxygen). This will result in a higher configurational entropy for the random coil (remember that phi/psi principles hold for the random coil as well).