

Biochemistry 461, Section I

Your Name: _____

March 19, 1998

Exam #2

Your SS#: _____

Prof. Jason D. Kahn

Your Signature: _____

Please have photo ID available.

You have 80 minutes for this exam.

Exams written in pencil or erasable ink will not be re-graded under any circumstances.

Some information which may be useful is provided on the bottom half of the page.

Explanations should be concise, no more than three or four sentences.

You will probably not need a calculator for this exam, no other study aids or materials are permitted.

Possibly Useful Information:

$$\Delta G = \Delta H - T\Delta S$$

$$i \approx i + 4$$

Ensigns suffice.

1. Secondary structure: α -helices, β -sheets (25 pts)

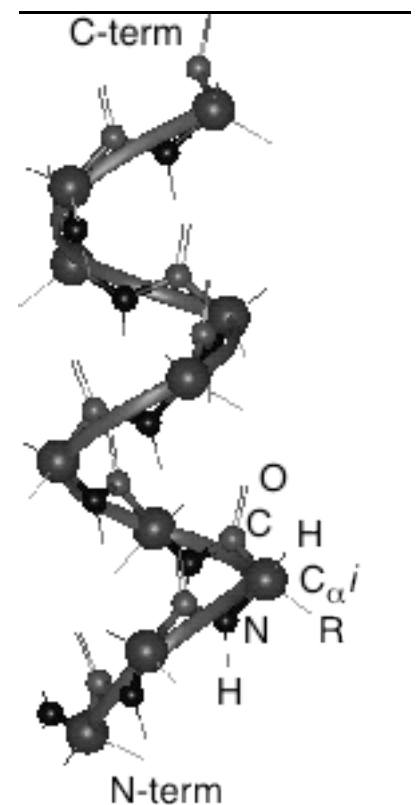
(a) (6 pts) List three general characteristics shared by stable secondary structures.

- (b) (10 pts) The sequence below has been shown by NMR to lie on the surface of a protein. Based on this location, on its sequence, and on your knowledge of secondary structure, is it more likely to be part of an α -helix or a β -sheet? Explain your reasoning. Which side will face the inside of the protein, and why?

...-His-Phe-Asp-Trp-Lys-Ile-Thr-Val-Ser-...

- (c) (7 pts) Using the drawing of the alpha helix backbone at the right, answer the following questions. (The alpha helix on the overhead is the same thing in color.)

1. Draw in the six backbone hydrogen bonds.
2. Circle the backbone of residue $i + 2$ (including its N, C $_{\alpha}$, and carbonyl carbon).
3. Indicate the direction of the dipole moment. Explain its origin:



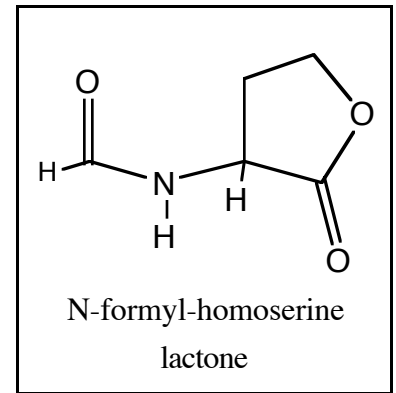
- (d) (2 pts) Why are active sites of enzymes typically not formed from single extended secondary structure elements?

2. Peptide chemistry and sequencing (18 pts).

A decapeptide (10-mer) is subjected to analysis with the results below:

1. Edman degradation: no products.
2. Cyanogen bromide gives a nonapeptide (9-mer) and N-formyl-homoserine lactone, shown at the right:
3. Trypsin digestion of the nonapeptide gives GDYR and a pentapeptide.
4. Carboxypeptidase A releases first V and then F.
5. One product of chymotrypsin digestion is RQLTF.

Scratch space:



- (a) (6 pts) What is the sequence of the peptide?
- (b) (2 pts) Why is the Edman degradation in step 1 unsuccessful?
- (c) (3 pts) A blocked Edman can be a real pain. What method, mentioned briefly in class, would you use to approach the general problem of sequencing blocked peptides?

- (d) (7 pts) Very briefly, how is the sequence of a purified but otherwise unknown protein from *E. coli* ~~or~~ *Saccharomyces cerevisiae* (yeast) most easily determined? The method I'm thinking of might be able to tell you about phosphorylation sites on the protein. How? If it didn't, what more difficult approach would you have to take?

3. Mechanism of protein folding (25 pts).

- (a) (17 pts) We used a helicopter skiing analogy for protein folding on the rugged energy landscape. In this sport of non-academics, one is lowered from a helicopter onto open mountainous terrain and skis down the mountain to a base camp in a valley below. What is the equivalent in terms of protein folding for each of the following parts of the analogy?
1. (1 pt) The skier.
 2. (2) The state of the skier while she is still in the helicopter.
 3. (1) The camp in the valley.
 4. (3) The topography of the mountains. In what way is this an oversimplification?
 5. (3) Skiing into a bowl and climbing back out.

6. (3) The ski patrol coming by in a snowmobile to drive the skier up to the lip of the bowl and letting her ski down. Is there an analogy that actually occurs for the ski patrol driving a tired skier back to camp? Why or why not?

7. (1) The gasoline in the snowmobile's tank.

8. (3) Twelve skiers who all crash into each other and knock each other unconscious at dusk in a snowstorm.

- (b) (2 pts) What sort of doctors was used to provide an analogy for the Levinthal folding paradox?

- (c) (6 pts) How does the Anfinsen experiment hold out the hope that we will someday be able to predict protein function from primary sequence?

4. Protein thermodynamics and stabilizing forces (20 pts).

- (a) (8 pts) The idea of entropy-enthalpy compensation for weak attractive interactions holds that as a weak interaction becomes stronger,

ΔH becomes more positive more negative stays about the same (circle one)

ΔS becomes more positive more negative stays about the same (circle one)

Why?:

ΔG becomes more positive more negative stays about the same (circle one)

Why?:

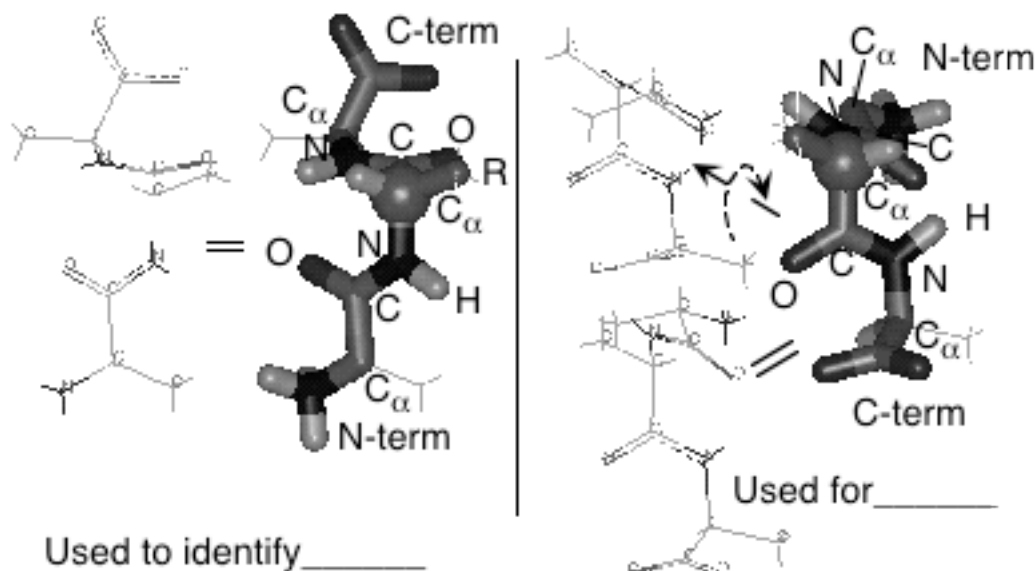
- (b) (5 pts) What is the physical rationale for the positive ΔH and positive ΔS associated with the transfer of non-polar solutes (e.g. alkanes) from water to organic solvents (e.g. CCl_4)? What is the name of this phenomenon?

- (c) (7 pts) Why don't proteins get cavities? Specifically, in terms of the thermodynamic forces stabilizing proteins, explain why an Ile $\rightarrow$ Ala mutation in the hydrophobic core of a protein tends to decrease T_m (i.e. make the folded protein less stable relative to unfolded).

5. Ramachandran diagrams and conformational analysis (12 pts).

The picture below is five different views of the same tripeptide. From looking at these pictures and at the color versions on the overhead, answer these questions concerning the ϕ , ψ angles of the central amino acid, indicated with the large C_α atom.

- (5 pts) Indicate which half of the picture and which four atoms (circle their labels) you used to determine the ϕ angle. Circle the correct value: $\pm 180^\circ$ -60° 0° 120°
- (5 pts) Indicate which half of the picture and which four atoms (circle their labels) you used to determine the ψ angle. Circle the correct value: $\pm 180^\circ$ -90° 90° 120°
- (2 pts) Draw parallelograms, one per thick-bonded diagram, to indicate six atoms constrained to be coplanar by the peptide bond.



Score:	Question 1:	_____	out of 25
	Question 2:	_____	out of 18
	Question 3:	_____	out of 25
	Question 4:	_____	out of 20
	Question 5:	_____	out of 12
	Total:	_____	out of 100