**BCHM 463** **Your Name:** _____

**Biochemistry and Physiology** **ID #:** _____

**Exam I, October 9, 2002** **Prof. Jason Kahn**

You have 50 minutes for this exam.

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

You may use a calculator for this exam. No other study aids or materials are permitted.

Generous partial credit will be given, *i.e.*, if you don't know, guess.

Explanations should be concise and clear. I have given you a lot more space than you should need.

Honor Pledge: Please write out the following sentence and sign it, or talk to me about it:

"I pledge on my honor that I have not given or received any unauthorized assistance on this examination."

## 1. "Bioinformatics" (20 pts):

(a; 15 pts) Homology search programs use similarity matrices like BLOSUM62 in assessing the likelihood that two sequences are homologous. List and briefly describe three elements, other than the simple fact of amino acid identity, that enter in to assigning a "score" for a given alignment. In other words, what aspects of our knowledge of protein structure and synthesis are embodied in the matrix and alignment procedures?

(b; 5 pts) A homology search is usually the first thing one does upon isolating a new gene/protein from a genetic screen. What is the most important thing one hopes to find out by doing this? Name a frequently-used homology search program.

## 2. Hemoglobin (25 pts):

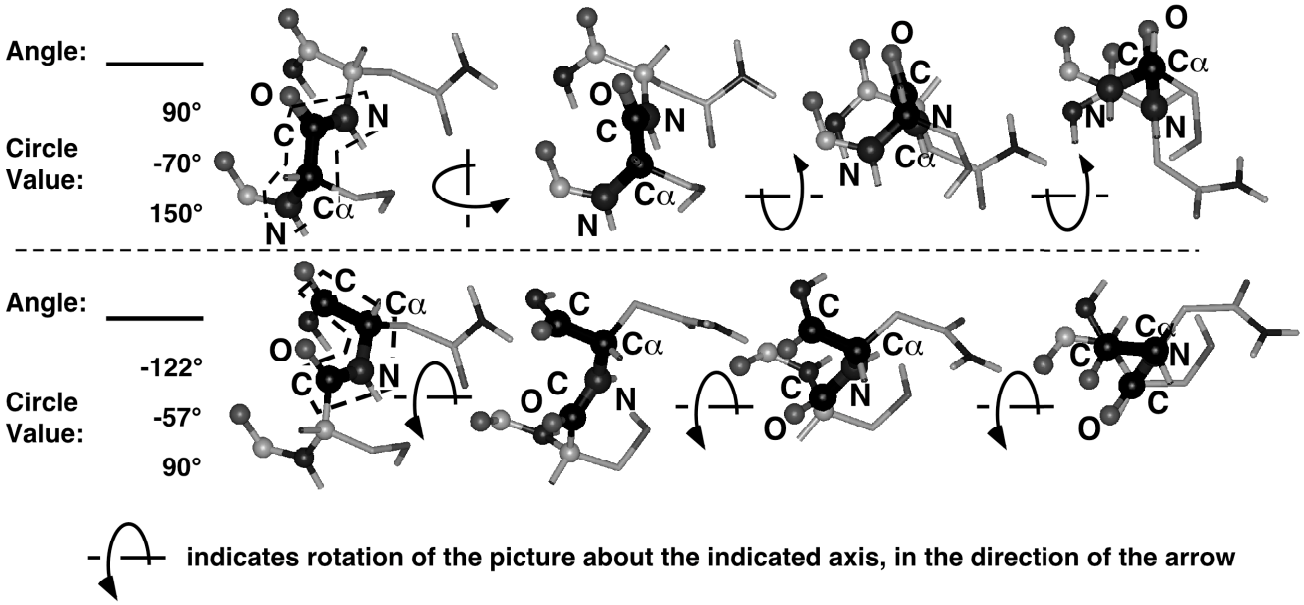
(a; 10 pts) When bicarbonate $HCO_3^-$ is produced in the red blood cell, it equilibrates across the membrane with the blood plasma. Charge neutrality requires that another anion must come in if bicarbonate goes out. This anion is chloride, $Cl^-$. Based on your appreciation of hemoglobin as a finely tuned oxygen delivery machine, do think that chloride will (a) promote $O_2$release or (b) promote $O_2$binding, and why? Given your answer, to which state of Hb (R or T) must the chloride bind more tightly?

(b; 10 pts) The Bohr effect refers to the release of protons upon $O_2$ binding to Hb. Much of the Bohr effect is due to a change in the $pK_a$ of the C-terminal histidine of the ß subunit (His 146ß). The $pK_a$ of this histidine is about 7.1 [actually it's 8] in the T state. Given this fact, calculate what percentage of the total His146ß is protonated at pH 7.4. In order for it to contribute to the Bohr effect, must the $pK_a$ of this residue go up or down upon conversion to the R state, and why? What sort of interaction in the protein could cause this effect?

(c; 5 pts) Draw the structure of the dominant prototropic form of the plain amino acid histidine at pH 4, including stereochemistry at $C_\alpha$.

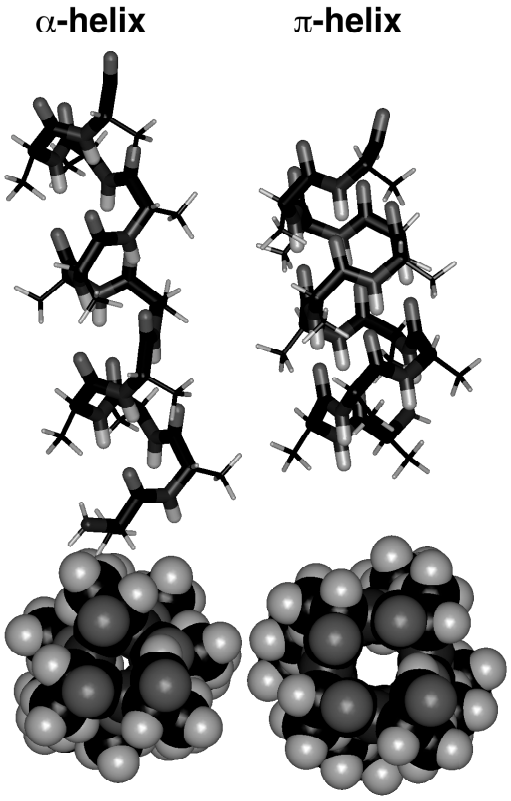
## 3. Ramachandran Angles and Secondary Structure (25 pts):

(a; 16 pts) The diagram below shows a peptide fragment in which all of the amino acids have the same Phi (Φ)and Psi (Ψ) angles. The overhead shows the same thing in color. All eight images are the same peptide in different orientations, with gradual rotations from left to right in each row. In the blank on the left, write which angle is defined by the four atoms represented by the thick bonds and boxed in the dashed line, and circle the correct value of that angle.




indicates rotation of the picture about the indicated axis, in the direction of the arrow

The fragment above is part of a conceivable secondary structure called the "Π-helix," which is shown on the right in comparison to the familiar Α-helix.



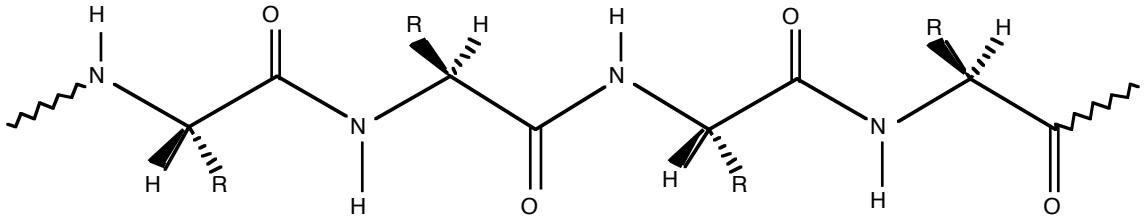

(b; 4 pts) The Φ and Ψ angles for the Π-helix are in an allowed part of the Ramachandran diagram. What does it mean to be in an allowed region?

(c; 5 pts) The □-helix is not, however, observed in real proteins. Based on your understanding of the principles of protein structure, why not?

## 4. ß Sheets: The Good, the Bad, and the Ugly (30 pts):

(a; 14 pts) Name a prion disease. Briefly describe what is known about the sporadic appearance and about the transmission of prion diseases. What is (some of) the evidence that the infectious particle has no nucleic acid component? Why are prions somewhat surprising in terms of how we normally think about protein folding?

(b; 10 pts) Draw in three residues of the antiparallel β-sheet partner below the extended polypeptide chain drawn here. Include Cα stereochemistry and backbone hydrogen bonds, and indicate where the next strand (i.e. if you were to draw a third one) would H-bond. Indicate side chains with R. Indicate the N terminus and the C terminus of the strand you draw.




(c; 6 pts) What are the steric interactions that cause the β sheet to be pleated? On your diagram above, indicated which Cα's will be pushed forward out of the plane, and which ones will be back.

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| Score: | 1. | "Bioinformatics" (20 pts): | _____ |
| | 2. | Hemoglobin (25 pts): | _____ |
| | 3. | Ramachandran Angles and Secondary Structure (25 pts): | _____ |
| | 4. | ß Sheets: The Good, the Bad, and the Ugly (30 pts): | _____ |
| | | **Total: out of 100** | _____ |