BCHM 463 **Your Name:** _____

Biochemistry and Physiology **ID #:** _____

Exam II, March 19, 2003 **Prof. Jason Kahn**

You have 55 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.

Hill equation: $Y_{O_2} = \frac{(pO_2)^n}{(p50)^n + (pO_2)^n}$

Explanations should be concise and clear. I have given you 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. Hemoglobin allostery and oxygen transport (35 pts):

(a; 10 pts) Briefly describe three steps, in terms of changes in protein and heme structure, in the allosteric induction of the R state of hemoglobin upon binding a molecule of O_2. What one word describes the shape of the resulting binding curve?

(b; 25 pts: 5 pts each) For each of the following ligands, indicate whether it binds better to the R state or the T state of hemoglobin, and briefly describe the significance of the preference to physiological oxygen transport.

O_2 (Circle one: R T) Significance:

H^+ (Circle one: R T) Significance:

CO_2 (Circle one: R T) Significance:

NO (Circle one: R T) Significance:

BPG (Circle one: R T) Significance:

2. Protein folding and prions (25 pts):

(a; 9 pts) What is the molten globule in protein folding? How does the activity of chaperones in unfolding molten globules enhance the overall rate of folding to the native state?

(b; 8 pts) Name a protein folding disease. Give two possible general causes for disease arising from protein folding defects.

(c; 8 pts) Give two rationales for the prevalence of independently folding 100-200 residue domains in proteins. How might you identify domain boundaries, either experimentally or by sequence analysis (pick one)?

3. Protein sequence analysis and evolution (25 pts):

(a; 6 pts) The sequence below shows three segments of a protein region that binds retinol, a large hydrophobic ligand. Do you think the binding region is an α-helix or a β-sheet? Explain your reasoning. (Exaggerated from the actual sequence given by Branden and Tooze.)

… Ile – Ala – Val – Glu – Phe – Ser – Val – Asp …
… Met – Ser – Ala – Thr – Val – Lys – Gly – Arg …
… Ala – Asp - Met – Val – Trp – Cys – Phe – Thr …

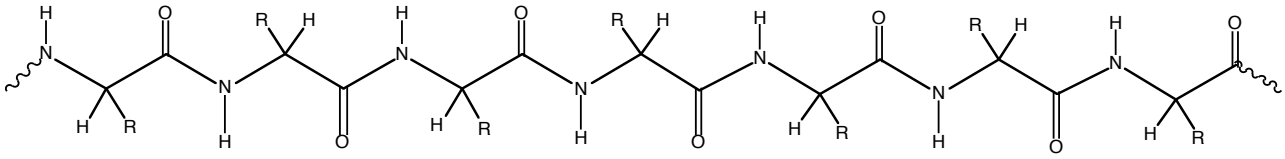
(b; 5 pts) Which is more conserved in evolution, primary sequence or tertiary structure? Why?

(c; 9 pts) How are protein sequences used in constructing phylogenetic trees? Why does the phylogeny of a protein sometimes not match up with the phylogeny of the organisms it inhabits?

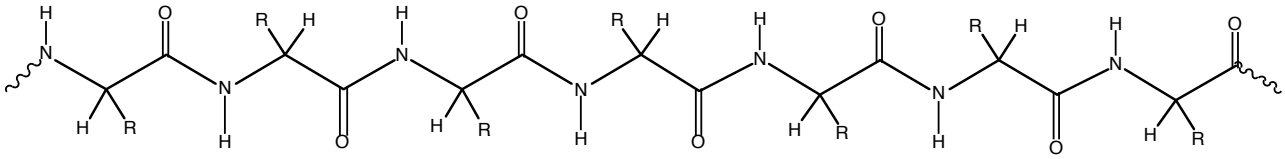
(d; 5 pts) How can the analysis of protein families improve homology searches? Name a program that extends BLAST in this way.

4. Secondary structure (15 pts):

(a; 6 pts) On the extended peptide representation below, diagram the hydrogen bonding pattern of the α-helix. In other words, draw in which three carbonyls are H-bonded to which three amides.



If you mess up, try again here:



(b; 5 pts) What is the number of residues per turn for the α-helix? The i → i ± (some number) H-bonding pattern you diagrammed in (a) connects amino acids that are one above another along the direction of the helix axis. How can this be consistent with a non-integral number of residues per turn?

(c; 4 pts) Why does leucine have a greater propensity to be found in the α-helix than isoleucine, whereas Ile has the greater β-sheet propensity of the two?

Score:	1.	Hemoglobin allostery and oxygen transport (35 pts):	_____
	2.	Protein folding and prions (25 pts):	_____
	3.	Protein sequence analysis and evolution (25 pts):	_____
	4.	Secondary structure (15 pts):	_____
		Total: out of 100	_____