Biochemistry 463, Summer II **Your Name:** Key

University of Maryland, College Park **Your SID #:**

Biochemistry and Physiology **Prof. Jason Kahn**

Exam I (100 points total) **July 27, 2009**

N=29

You have 80 minutes for this exam.

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

Explanations should be concise and clear. I have given you more space than you should need. There is extra space on the last page if you need it.

You will need a calculator for this exam. No other study aids or materials are permitted.

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

Useful Equations:

$\Delta S_{system} - \Delta H_{system}/T \geq 0$ $\quad pH = -\log([H^+])$ $\quad E = mc^2$

$S = k\ln W$ $\quad \Delta G = \Delta H - T\Delta S$ $\quad pH = pK_a + \log([A^-]/[HA])$

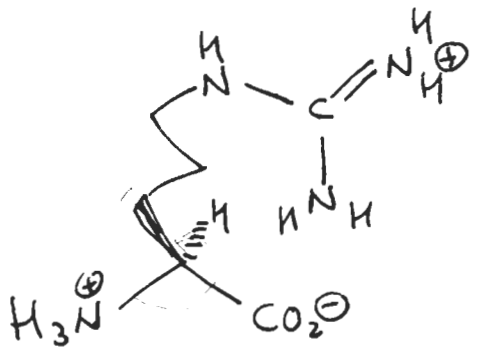
$K_a = [H^+][A^-]/[HA]$ $\quad \Delta G° = -RT\ln K_{eq}$ $\quad e^{i\pi} + 1 = 0$

Honor Pledge: At the end of the examination time , 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. (35 pts) Amino acid structure and the peptide bond

(a; 8 pts) Draw the structure of arginine in its predominant ionic form at pH 7, including the stereochemistry at Cα. Give its three-letter and one-letter codes. Give the name of the other amino acid that is positively charged at pH 7.



+1 for any amino acid
+2 for guanidinium
+1 for charges
+1 for Cα chirality
+1 for correct # of carbons

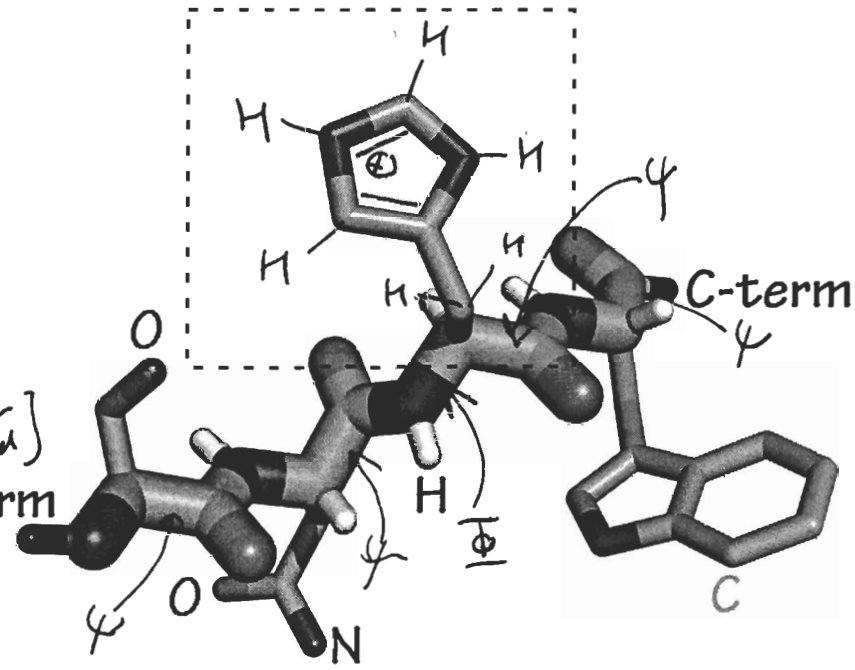
+2 Lysine [+1 for Lys, 1C]

Score for the page_____

(b; 4 pts) Why is it important to life that all amino acids in proteins have the same stereochemistry at Cα, as opposed to a random stereochemistry?

- If the stereochemistry were random, for an N-residue protein there would be 2^N (many!) diastereomers. (+2)
- The proteins would all be inactive. (+2)

The diagram at the right shows a tetrapeptide. Each amino acid has the same pair of Φ and Ψ angles. The backbone is thickened for your convenience. Side chain hydrogens are not shown.



(c; 4 pts) Give the sequence of the peptide, using three-letter codes: (+1 each) [+2 for order reversed]

N Ser-Asn-His-Trp C

(d; 3 pts) Fill in all the hydrogens that one would find inside the ~~dashed box~~ at pH 4.

(+½ point each, round down)

(e; 4 pts) Indicate on the diagram one bond that defines a Φ angle and one that defines Ψ (i.e. the bonds that ~~one would~~ look down to measure Φ or Ψ).

(+2 each) C–Φ–C N–Ψ–N

(f; 3 pts) Circle the correct ~~Φ/Ψ~~ Φ/Ψ pair: (–120°/120°) 0°/180° –60°/90° 120°/–60°

+2 +3

+1 for any attempt at a Newman projection if answer is wrong

Score for the page_____

(g; 4 pts) Does this conformation look like it is in an allowed region of the Ramachandran plot? Why or why not?

Yes - no obvious steric hindrance - ~~ex~~ extended

+1 +3

(h; 5 pts) If this peptide conformation was part of a regular secondary structure, which one would it be and why?

(+2) β-sheet - i → i+4 clearly can't happen, but H-bond donors + acceptors are roughly (+3) parallel or it's an extended conformation or you remember where the allowed β-sheet region is on the Ramachandran diagram

2. (40 pts) Protein Folding

(a; 6 pts) Why are enzyme active sites typically formed at crevices on the surfaces of proteins rather than deep inside or on a convex surface, and why are active site residues typically not neighboring residues in regular secondary structures?

+3 - To make specific contacts requires enough surface area to contact several parts of the substrates.

+3 - In regular 2°s the side chains point away from each other and can't ~~cluster~~ cluster around.

(b; 3 pts) What is the advantage of using the BLOSUM62 for BLAST searches, instead of just looking at whether amino acids in putative homologs are identical?

+3

The Blosum matrix considers chemistry as well as just sequence conservation at the DNA level - it considers which mutations are most likely to be tolerated

Score for the page_____

Part of the BLOSUM matrix from the text is shown below:

(c; 3 pts) Why is the score for replacing Cys with Cys higher than the score for Ala to Ala (in other words, why is it more meaningful to find Cys in the same place in two potential homologs than it is to find Ala?)

+3 Cys is a rare amino acid - (less likely to appear by chance. Ala is common

(d; 3 pts) Why are there no replacements for Cys that contribute a positive score whereas there are several high-scoring replacements for Ile?

It's the only thiol whereas Ile can be replaced by other bulky hydrophobics

+3 Cys has unique ability to form disulfides, metal ligand, etc.

(e; 2 pts) Why is Val a better replacement for Ile even though Leu has the same molecular formula?

β-branching vs.

+2 γ-branching of Leu.

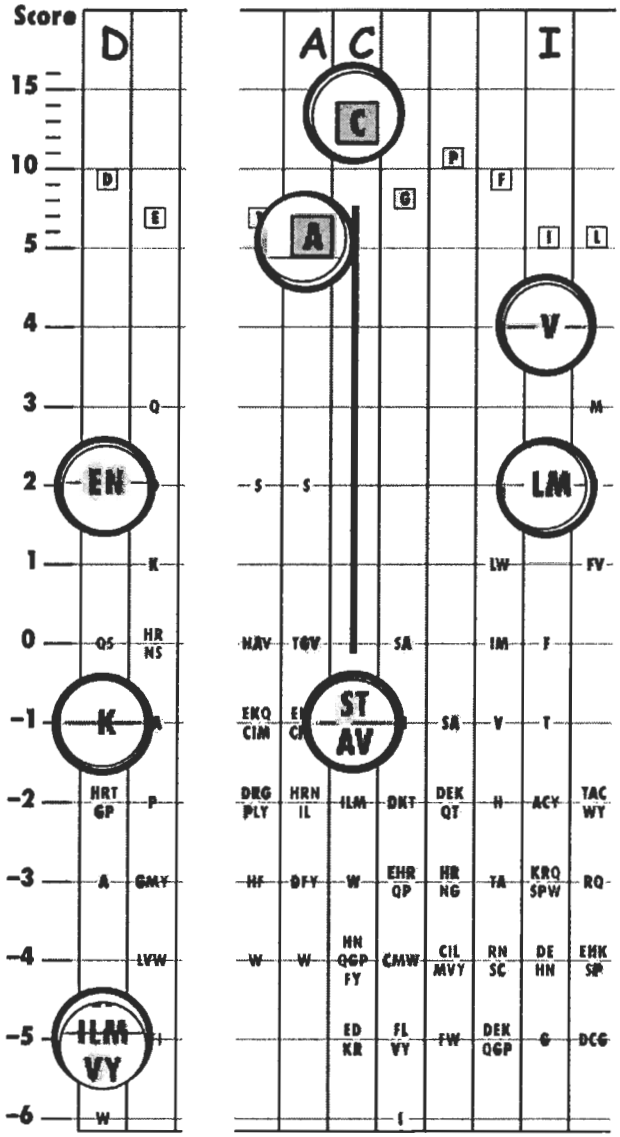


Figure 6-9
Biochemistry, Sixth Edition

(f; 3 pts) Why is K, perhaps surprisingly, a more likely replacement for D than I, L, M, V, or Y?

If it's on the surface the charge doesn't matter

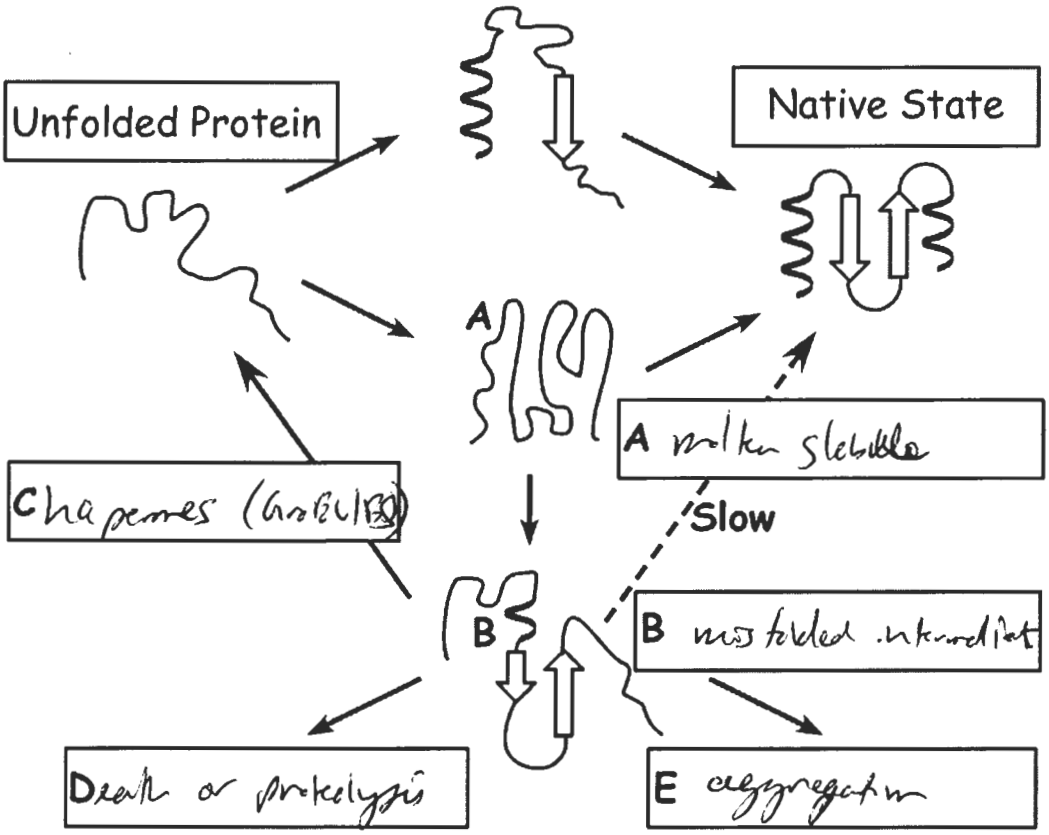
+3 but it can't be replaced by a hydrophobic residue.

Score for the page_____

The sketch below summarizes possible futures for the unfolded protein at the top left.

(g; 10 pts)
Identify on the sketch (write their names):
Possible folding intermediate (A)
State (B), which is analogous to a skier trapped at the bottom of a hill without a lift.
Protein or activity (C) that takes (B) back to Unfolded Protein
Two terminal fates (D) and (E)

+2 each



(h; 3 pts) What particular feature of state (B) that differs from the native state targets state (B) to paths (C), (D), and/or (E)?

+3 exposed hydrophobic surface

(i; 7 pts) How does the nanomachinery identified as (C) use the free energy of ATP hydrolysis to give proteins a second chance to fold?

+2 | The exposed hydrophobic surface binds hydrophobic
+3 | areas in the Anfinsen cage. The energy of ATP
+2 | hydrolysis powers conformational changes that remove the h-phobic surface to release the substrate protein and allow it to fold again.

Score for the page_____

3. (25 pts) Biomolecules and Miscellaneous:

(a; 3 pts) Give a redox-based explanation for why fat is a denser source of dietary calories than carbohydrates.

+2 There are more electrons per carbon available to be given to oxygen.

+1 The average redox state of C in fat is -2, in carbohydrates it is 0.

(b; 3 pts) Membranes undergo a transition from a liquid crystalline state to a more fluid state as the temperature increases. What does this simple observation tell us about the signs of ΔH and ΔS for forming the crystalline state?

If the L.C. state is stabilized at low T but melts out at high T, $\Delta G = \Delta H - T\Delta S$ tells us that $\Delta H < 0$ and $\Delta S < 0$, for fluid → L.C. — makes sense - bonds are formed in crystalline state.

+1 for one right, +3 for both

(c; 3 pts) Bacteria make more *cis*-unsaturated fatty acids as the growth temperature decreases in order to increase membrane fluidity. Why do you think they make more saturated fatty acids as temperature goes up, i.e. what would be wrong with just using more *cis*-unsaturated fatty acids at all temperatures?

+3 The membrane would lose structural integrity and be more likely to leak or burst.

(d; 6 pts) We gave three main functions for carbohydrates in biology. List them and give an example of each.

Fuel - glucose

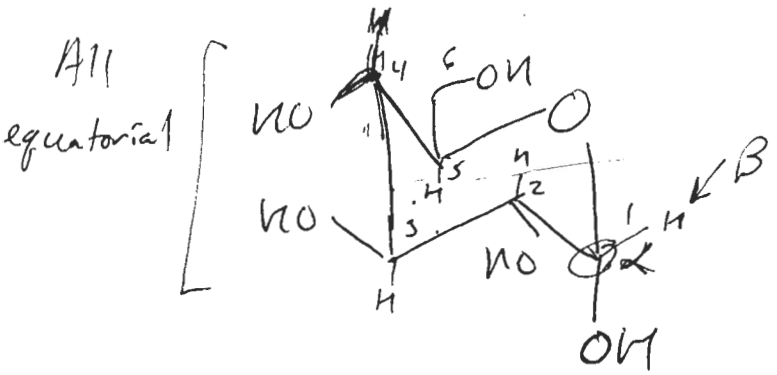
Structure - cellulose or cell wall

Information - glycoproteins or glycolipids

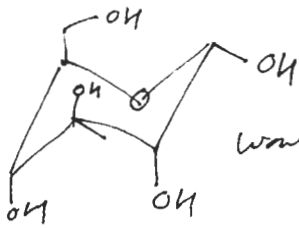
+1 each

Score for the page_____

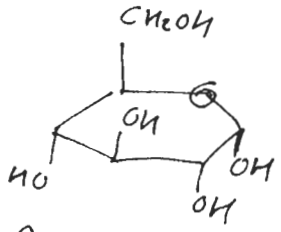
(e; 5 pts) Draw the structure of α-D-glucopyranose in the chair form.



+2 for a pyranose [+1 for 6-ring, +1 for O in the ring]
+2 for alpha
+1 for HO's correct other



would be much less stable



(f; 5 pts) Calculate the ratio of $[ONO^-]/[HONO]$ at pH 4.5 for nitrous acid, HONO, pKa 3.25.

$$pH = pKa + \log \frac{[A^-]}{[HA]}$$ (+1)

$$4.50 = 3.25 + \log \frac{[ONO^-]}{[HONO]}$$ (+2)

$$\frac{[ONO^-]}{[HONO]} = 10^{1.25} = 18$$ (+2)

$10^{1.25}$ = $10^1 \times 10^{0.25}$

two sig figs

(extra credit; 1 pt) What does TANSTAAFL stand for?

There ain't no such thing as a free lunch!

Page	Score
1	/8
2	/18
3	/18
4	/11
5	/20
6	/15
7	/11
Total	**/101**

Score for the page_____