

BCHM 463

Your Name: Key

Biochemistry and Physiology

ID #: \_\_\_\_\_

Exam I, February 28, 2003

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.

Henderson-Hasselbach:  $\text{pH} = \text{pK}_a + \log \left( \frac{[\text{A}^-]}{[\text{HA}]} \right)$  ← Gibbs free energy:  $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$

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

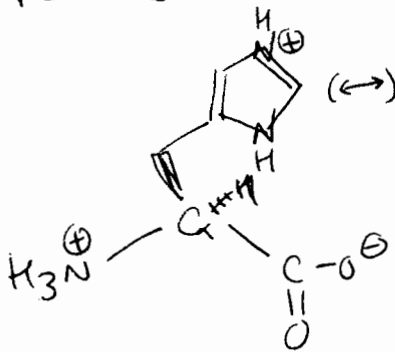
**(2 pts) Honor Pledge:** Please write out the following sentence and sign it, or talk to me about it:

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

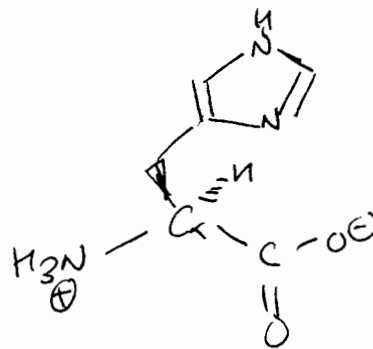
### 1. pH, pK<sub>a</sub>, and all that (25 pts):

(a; 9 pts) The imidazole side chain of histidine has a pK<sub>a</sub> of 6.04 (referring to the protonated side chain). Draw the dominant prototropic forms of histidine at (1) pH 4, (2) pH 8, and (3) pH 12.

pH 4

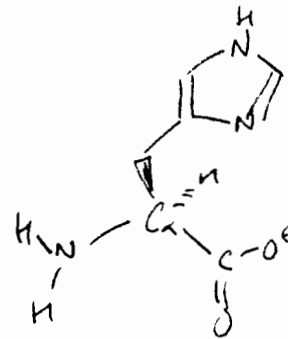


pH 8



this is the correct tautomer - but either is fine

pH 12



(+1) for an amino acid

(+2) for histidine side chain

(+2) for each correct protonation state (=6)

↳ *i.e.* all three correct at a given pH

(b; 6 pts) Calculate the ratio of neutral to protonated histidine at pH 6.5.

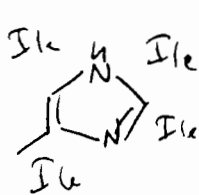
$$pH = pK_a + \log \frac{[A^-]}{[HA]} \quad (+1)$$

Here,

$$6.5 = 6.04 + \log \frac{[His]}{[HisH^+]} \quad (+3)$$

$$\log \frac{[His]}{[HisH^+]} = 0.46 \quad \frac{[His]}{[HisH^+]} = 10^{0.46} = \underline{2.88} \quad (+2)$$

(c; 10 pts) We have mentioned that the  $pK_a$  of an amino acid side chain can change substantially in different protein contexts. If a histidine side chain were found buried among isoleucines in the center of a protein, what effect would this have on the actual  $pK_a$  of that particular side chain, and why? What if there were a buried aspartate as well?



- The hydrophobic environment will favor the neutral form of histidine. The charge side chain would much rather be in  $H_2O$ . (+3) for hydrophobic of charge

- Therefore  $HisH^+$  will become a stronger acid, corresponding to a lower  $pK_a$ , larger  $([His]/[HisH^+])$ . (+3)

- A neighboring negatively charged aspartate, in contrast, will strongly stabilize  $HisH^+$ , and the  $pK_a$  will increase. (+2) for opposite  
 [The  $pK_a$  of the Asp ~~would~~ <sup>would</sup> ~~be~~ <sup>be</sup> if it were considered ~~alone~~ <sup>alone</sup> (+1) if neutral, or (+2) if other site missed

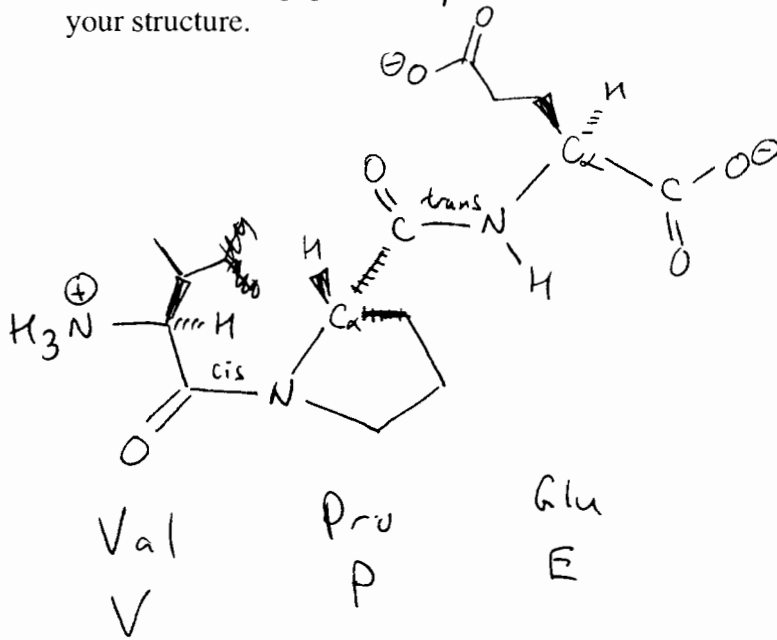
**2. Amino acid and peptide bond structure and chemistry (26 pts):**

(a; 6 pts) Name the two sulfur-containing amino acids, and very briefly list one unique function for each.

Cysteine and methionine  $\rightarrow$  inhibition of protein biosynthesis, as f-Met (+2)  
 $\hookrightarrow$  Disulfide crosslinks (+1)

+1 for either one for protein radiolabeling

(b; 15 pts) Draw the structure of Valine-Proline-Glutamate at pH 7. Make the proline peptide bond *cis* and the other peptide bonds *trans*. Give the 3- and 1-letter codes for each amino acid below your structure.



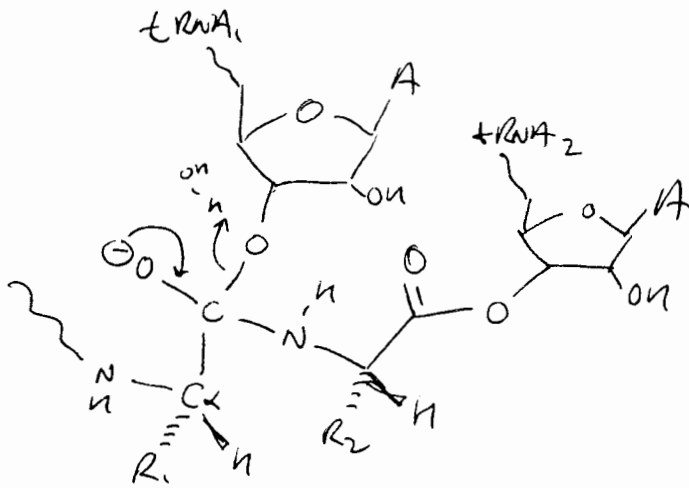
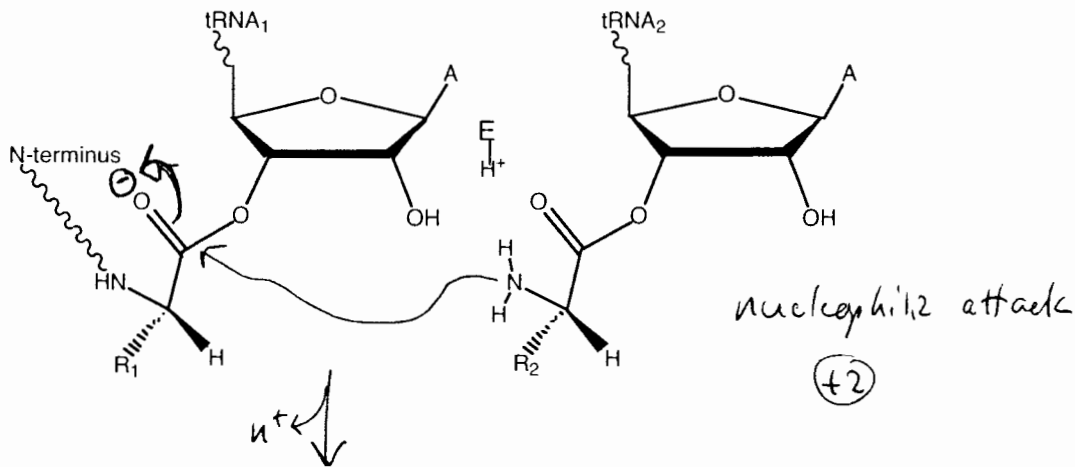
- (+2) for any tripeptide
  - (+2) for each side chain = 6
  - (+2) for cis peptide bond
  - (+1) for  $\ominus$  charge on Glu
  - (+1) for charges on both termini correct
  - (+1) for each correct pair of labels (=3)
- 
- 15

Stereochemistry not graded.

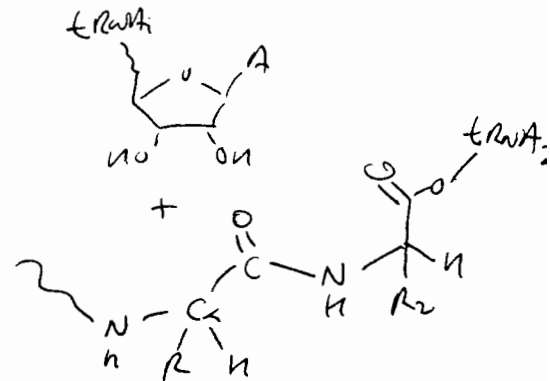
Difficult to draw because Pro is non-planar

Everything but the cis-proline = 13 pts total

(b; 5 pts) The structure below shows two charged tRNA molecules aligned for the process of peptide bond synthesis. Draw the first step of the reaction mechanism.



(+3) tetrahedral intermediate  
or product (+2)



3. Thermodynamics (25 pts): <sup>biological</sup>

(a; 6 pts) What are the two most important functions for lipids?

- (+3) - Biomembranes - phospholipids
- (+3) - Fuel - fatty acids

(b; 9 pts) Briefly describe how cells maintain order in the face of the universal tendency toward increasing entropy.

- Cells take in ordered molecules like glucose.
- They ~~use~~ <sup>couple</sup> the favorable free energy of fuel oxidation (combustion) to the unfavorable decrease in entropy associated with biosynthesis, growth, and reproduction.

+3 |

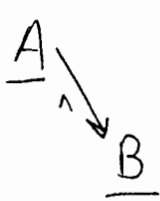
(+1 each for idea of coupling down + come through)

- The favorable catabolic reactions lead to production of CO<sub>2</sub> gas, with much greater entropy than glucose, and also heat (CO<sub>2</sub> is enthalpically very stable as well), which ~~de~~ ↑ entropy of the universe. Don't need details of giving off CO<sub>2</sub> - just specify less ordered waste products.

+3 |

+3 |

(c; 10 pts) You have discovered an enzyme that converts substance A to substance B without requiring any input of free energy (i.e. the reaction proceeds without high-energy cosubstrates like ATP). The equilibrium lies far to the side of B. What then must be true about any process that carries out net conversion of B to A under the same conditions? Also, explain why your discovery either does or does not preclude the possibility that there may be a separate energy-consuming path for going from A to B, and a biological rationale for your answer.



(+1) downhill → the reverse B → A process must be thermodynamically unfavorable, uphill. (+2)

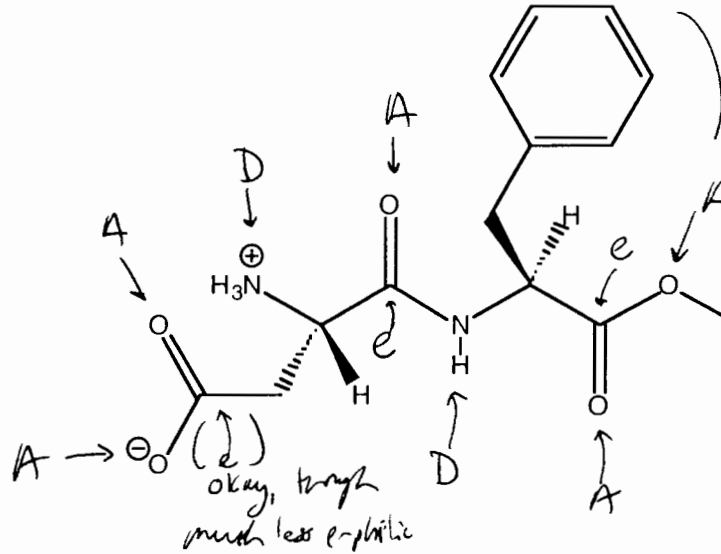
(+3) Therefore B → A must be coupled to an exergonic reaction like ATP hydrolysis.

A → B can go via an energy-consuming back (drive the car downhill under power), would be done for greater speed, specificity, and/or control. (+2) for any one

4. Intermolecular interactions(22 pts):

(a; 12 pts) The structure of the artificial sweetener Aspartame is shown below. Identify potential hydrogen bond donors and acceptors, and electrophilic carbons. Why must phenylketonurics avoid Aspartame? (Memory jogger: would Aspartame absorb UV light?)

A = acceptor  
 D = donor  
 e = electrophile



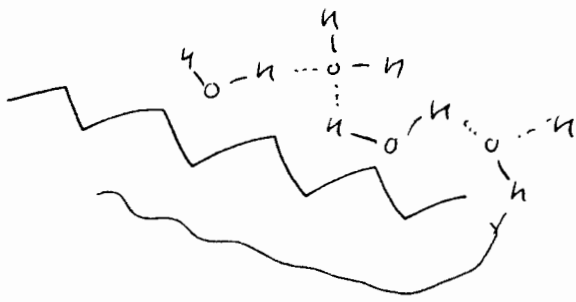
Phenylalanine = Phe

- +1 for idea of H-bonds
- +2 for mostly correct D/A
- +1 for correctly identifying all the D/A
- +1 for no H-bond to aliphatic H's
- +2 for electrophiles

- Aspartame is metabolized to give phenylalanine. PKU sufferers cannot convert Phe → Tyr, and toxic by-products ~~and~~ accumulate.

(+3)  
 +1 for Asp would absorb UV if missed PKU question

(b; 10 pts) Briefly describe the origin of the hydrophobic effect. Give the signs of  $\Delta H^\circ$ ,  $\Delta S^\circ$ , and  $\Delta G^\circ$  for the process of dissolving a long alkyl chain in water.



- water forms an ordered cage around hydrophobic solutes. This is unfavorable - aggregation of the solutes (or phase separation) (3)

(2) leads to release of H<sub>2</sub>O into more disordered bulk water and is the driving force for the fact that oil and water don't mix.

(2)  $\Delta H^\circ$  is  $\ominus$   $\rightarrow$  the clathrate cage is enthalpically favorable!

(1)  $\Delta S^\circ$  is  $\ominus$   $\rightarrow$  because of ordering of water

(2)  $\Delta G^\circ = \Delta H - T\Delta S$  is  $\oplus$   $\rightarrow$  process is not spontaneous

Score: 1. pH, pK<sub>a</sub>, and all that (25 pts): \_\_\_\_\_

2. Amino acid and peptide bond structure and chemistry (26 pts): \_\_\_\_\_

3. Thermodynamics (25 pts): \_\_\_\_\_

4. Intermolecular interactions (22 pts): \_\_\_\_\_

**Total: out of 100 (2 pts for Honor Pledge)** \_\_\_\_\_