Names:  
1. Where appropriate, show work to receive full credit.  
2. This exam contains 10 pages.  
3. Pace yourself - you may want to do the easiest questions first.  
4. Note the point value of questions varies widely - adjust your answers accordingly.  
5. Please give concise answers - unfocused, rambling, answers often receive less credit than a few short phrases. If there isn't much space allotted - a short answer is appropriate.  
6. Some questions have more data than needed to tackle the problem.  
7. FINALLY PLEASE write clearly. If we cannot read it .... it is wrong.

<table>
<thead>
<tr>
<th>Name</th>
<th>pK αCOOH</th>
<th>pK αNH</th>
<th>pK (β-R)</th>
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<tr>
<td>Alanine</td>
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<td>9.7</td>
<td>-</td>
</tr>
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<td>9.0</td>
<td>12.5</td>
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<td>-</td>
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<td>9.1</td>
<td>-</td>
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<tr>
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<td>9.7</td>
<td>4.2</td>
</tr>
<tr>
<td>Glycine</td>
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<td>9.6</td>
<td>-</td>
</tr>
<tr>
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<tr>
<td>Valine</td>
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</table>
Question 1 (15 pts). Short problems. Most of the credit goes for the correct numerical answer.

a. The pH of a solution is 3.3. What is the hydroxide ion concentration?

\[
\begin{align*}
[H^+] &= 10^{-3.3} \\
[OH^-] &= \frac{10^{-14}}{10^{-3.3}} \\
[OH^-] &= 10^{-11.7} \\
[OH^-] &= \frac{9.95 \times 10^{-11}}{M}
\end{align*}
\]

b. Aspirin (pK 3.5), a weak carboxylic acid, is dissolved in water to give a solution with a pH of 2.5. What concentration of aspirin was used?

\[
[H^+] = 10^{-2.5} = 3.16 \times 10^{-3} M \quad \text{[aspirin]} = \frac{3.16 \times 10^{-2}}{M}
\]

Thus \([A^-] = \text{same}\)

So: \(2.5 = 3.5 + \log\left(\frac{3.16 \times 10^{-3} \text{M}}{3.16 \times 10^{-2} + 3.16 \times 10^{-3} \text{M}}\right)\)

\(\text{Shayley should have } 3.16 \times 10^{-3}\)

C. You add 0.19 moles of KOH to 0.5 L of 0.4 M formic acid (pK 3.7). What is the pH of the mixture?

\[
\text{Amount formic } = 0.5 L \times 0.4 \text{ mol/L} = \frac{1}{2} \text{ mol}
\]

\[
\text{pH} = 3.7 + \log\left(\frac{0.01}{0.19}\right) = 4.9788
\]

D. A 100 residue protein with 5 disulfide bridges is reduced and then disulfides are allowed to reform under denaturing conditions. How many possible disulfide combinations are possible?

\[
\text{Number} = 945
\]

E. You add 0.25 moles of \(\text{K}^+ \text{H}_2\text{PO}_4\) to 0.5 moles of \(\text{K}^+ \text{HPO}_4^{2-}\) in 1 L of water. The pK of the phosphate species here is 7.2. What is the pH of the mixture?

\[
\text{pH} = 7.02 + \log\left(\frac{0.5}{0.25}\right) = \frac{7.501}{\text{L}}
\]
Figure 2 (13 pts) The figure below depicts the crystal structure of “WIND”. WIND is a protein involved in the development of multicellular organisms. WIND is a dimer of identical subunits. Answer the questions as directed.

a. In the chain starting with an A (the N-terminus) what is the term for sections A-B and C-D?

b. Suppose A-B and C-D were also obtained as separate folded proteins (by expressing the fragments in bacteria). After denaturation in 8 M urea, which would you expect to fold fastest. Circle: A-B or C-D

Why? (one phrase on one line):
From class helices fold faster than sheets...

c. Draw the chemical structure of urea 

\[ \text{NH}_2 - \text{C} - \text{NH}_2 \]

d. The protein fragments (A-B and C-D) were found to differ in molecular weight when evaluated separately on gel-filtration in buffer. Which is likely to be a dimer. Circle one:

A-B or C-D or insufficient information

(3.6x4)

e. How many amino acids would you expect between positions E and F? 

f. How many H-bonds are likely to stabilize the structure between E and F

\[ 14 \pm 2 \]

\[ \sim 14 \pm 2 \]
g. What amino acid is likely to be at position G

h. Is J (in the figure on the previous page) an N-terminus or a C-terminus? Circle one: N-terminus C-terminus cannot say/insufficient information

i. The two segments labeled H and I are: circle all appropriate answers

Parallel beta stands Antiparallel beta strands Coiled coil Triple helix

Question 3 (10 pts) You have 0.2 mol of arginine (shown) in this particular ionic form dissolved in 1 L of water. Answer the following questions first circling the reagent (KOH or HCl) and then the amount you will need to get from the form shown to the indicated pH.

a. From original solution to a pH of 2.2 ___ mol of
   KOH or HCl (circle one)

b. From original solution to a pH of 9.0 ___ mol of
   KOH or HCl

c. From original solution to a pH of 12.5 ___ mol of
   KOH or HCl

d. From the original solution to a pH of 5.6 ___ mol of
   KOH or HCl

e. Circle the charge on arginine at pH 1 → 2 1 0 -1 -2

f. Circle the charge on arginine at pH 14 → 2 1 0 -1 -2
Question 4 (8 pts.) Draw the peptide cys-asp-gly-lys in the form that predominates at pH 6.0. Depict every atom in your drawing.

[Diagram of peptide structure]

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Question 5 (21 pts) Give the 3-letter abbreviation for the sequence: NEWTS

a. ASN GLU TRP THR SER

b. what is the electrical charge on NEWTS (assume the same side chain pK values as in the Table on first page. E has a side chain of -CH₂-CH₂-COOH)

at pH 12

-2

(1)

NEW a (ASN-GLU-TRP)

(1)

c. NEWTS is attacked by a proteolytic enzyme, named

CHYMOTRYPSIN

(1)

d. List the LARGEST fragment formed in "c"

NEW

(1)

e. How special is the NEWTS sequence? How many possible peptides of 5 amino acids could be synthesized if you could pick from 20 amino acids at every position (i.e. NNNNN is one of the sequences).

# $3.2 \times 10^6$

$20^5$

$\binom{20}{5}$

(3,200,000)
f. would this sequence often occur by chance in a protein of 500 amino acid residues? Circle one:

   yes [ ] no [ ] insufficient information [ ]

1. below is a sequence of an envelope glycoprotein from Human immunodeficiency virus 1. Inspect the sequence shown below (a single chain of 180 amino acids) and answer the following questions.

   1. IKPVSTQLLLGSLAEEBIIIPNITNNAKIIIVQLNSTITICTPRYQSPQRRSHIG

   LGRAYTTRIQGNIQICHNISEIGWNRTLQQVAKKLRLDYNTKIPFSSGGDPEITT

   HSFNCGEEFFCMTSGFLFNNNEDTSVTSTGVEDTDIIIPCHKQIINMOMGQVGK 180

i. clearly underline the newts sequence in the protein above.

ii. what are the maximum number of disulfide bonds that could form in a monomer of this protein?

      disulfides per monomer (a number from 0 - 10)

      2

iii. if this envelope glycoprotein were a dimer, what is the maximum number of disulfide bonds that could form in the dimer

      disulfides per dimer (a number from 0 - 20)

      5

iv. In the top line of sequence (residues 1-60) give the first 4 amino acids of the largest tryptic peptide (assume that the protein was reduced/alkylated first)

      IPPPV

v. In the entire sequence write below the shortest fragment generated on CNBr treatment of the envelope glycoprotein

      WQGVGK

      But note: the bond wait hydrolyze

      "CTRP4QSC"
Question 6 (6 pts) A buffer, pK 8.5, was being used at a concentration of 5 mM to maintain a protein solution at pH 8.9. The solution was stored exposed to air at 4 °C and the pH kept on dropping (... it was pH = 8.2 after 2 days).

Explain why (one line) - with appropriate chemical equations. In addition to using chemical notation please also give the chemical names for the compounds you draw.

Why: \( \text{CO}_2 \) from air dissolves to form carbonic acid which dissociates

\[
\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^- \quad \text{(carbon dioxide)} \quad \text{(carbonic acid)} \quad \text{(bicarbonate)}
\]

Question 7 (7 pts) Maximum of one line of text per answer. Please write legibly.

a. What is a significant disadvantage of peptide sequencing by mass spectrometry (apart from the cost of the instrument!): 

   Cannot distinguish LEUCINE from ISOLEUCINE

b. Name a program you might use to see if the amino acid sequence SLYSPSDPLELLGADTAERRLL is found in the chicken (and its translated genome).

   BLAST: basic local alignment sequence tool

   (SearchGenS27 web)

c. Identify the amino acid change in a mutation that causes brittle bone disease(s) (osteogenesis imperfecta)

   The mutation from amino acid GLY to SER

   And the molecular reason that this mutation is harmful/fatal:

   SER side chain disrupts interaction of triple helix normally accommodating GLY
Question 8 (9 pts) Referring to the graphs below, deduce the schematic structure of the proteins A-C. Using the sample answer for the amount of detail required, show the quaternary structural arrangement including disulfide linkages (if appropriate). The triangles on the graph to the right indicate the behavior of proteins A-C.

SDS-PAGE

<table>
<thead>
<tr>
<th>Protein A</th>
<th>Protein B</th>
<th>Protein C</th>
</tr>
</thead>
<tbody>
<tr>
<td>180 kDa</td>
<td>180 kDa</td>
<td>180 kDa</td>
</tr>
<tr>
<td>160 kDa</td>
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<tr>
<td>10 kDa</td>
<td>10 kDa</td>
<td>10 kDa</td>
</tr>
</tbody>
</table>

+/− β-mercaptoethanol

Gel filtration in buffer

Elution volume →

(−1 each significant error)

Sample answer

Protein A

No disulfides

Protein B

Protein C

Indicate disulfides where appropriate

38 48 kDa

15 kDa

15 kDa
Question 9 (6 pts) The structure of the analgesic lidocaine hydrochloride is shown (pK 7.9).

Predict the approximate pH values that would ensure a rate of absorption across a biological membrane that is:

a. 10% of the maximal rate

\[ \frac{A^-}{A^- + HA} = 0.1 \]

\[ \text{Strictly} \quad \frac{A^-}{HA} = \frac{1}{9} \]

\[ \text{pH} \quad 6.9(5) \]

\[ \text{pH} = \text{pK} + \log \frac{A^-}{HA} \]

b. 90% of the maximal rate

\[ \frac{A^-}{HA} = \frac{9}{1} \]

\[ \text{pH} \quad 8.9(8.85) \]

\[ \text{pH} \quad \text{unit} \uparrow \text{pK}, \frac{A^-}{HA} \]

\[ \text{pH} \quad 7.9 \]

Question 10 (5 pts) Using the table answer the following questions.

<table>
<thead>
<tr>
<th>PROTEIN</th>
<th>overall MW (native MW)</th>
<th>pl</th>
<th>#subunits</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>160,000</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>B</td>
<td>40,000</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>C</td>
<td>39,000</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>D</td>
<td>20,000</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

In the spaces provided put proteins A-D as appropriate, (you can use an answer multiple times). None of the proteins contains disulfide bridges.

The protein sticking tightest to an anion exchange (+ charged resin) at pH 7

The protein sticking tightest to a cation exchange resin (at pH 7)

The protein running fastest on SDS-PAGE

The protein running slowest on gel filtration in non-denaturing conditions

The protein with the largest proportion of ARG+LYS (compared to ASP+GLU)