CHEM-342 Introduction to Biochemistry Name _____
Midterm Examination - Individual Part
Wednesday, 26 March 2008
H. B. White - Instructor

Important - Please read this before you turn the page.

There are 9 pages to this examination including this page and the blank final page.

Write your name on every page.

This individual part of the midterm examination is worth 99 points with 7 bonus points possible.

There are 11 questions of which you need to answer 7.

You may refer to your notes, course reader, handouts, or graded homework assignments. Textbooks and reference books cannot be used.

This examination will assess your learning, problem-solving skills, and ability to communicate clearly. It is intended to be challenging even to the best students in the class.

Writing reflects how you think. Better quality answers will receive higher marks. Therefore organize your thoughts before you write and draw. Among the "right answers" I will read for the following questions, some will be better than others because they

- show greater depth of understanding,
- provide a more logical structure,
- use appropriate examples,
- include appropriate illustrations,
- avoid extraneous or inaccurate information, and
- choose words with precision.

Strive to write not that you may be understood, but rather that you cannot possibly be misunderstood. Stream of consciousness answers are rarely well organized or clearly presented.

1. (15 Points) Stokes observed the changes on the color of blood extracts after various treatments to deduce changes that had occurred. Based on your understanding of hemoglobin and its reactions described by Stokes and in class, predict the color changes expected when each of the following is done to a freshly drawn sample of blood to which citrate or heparin was included.

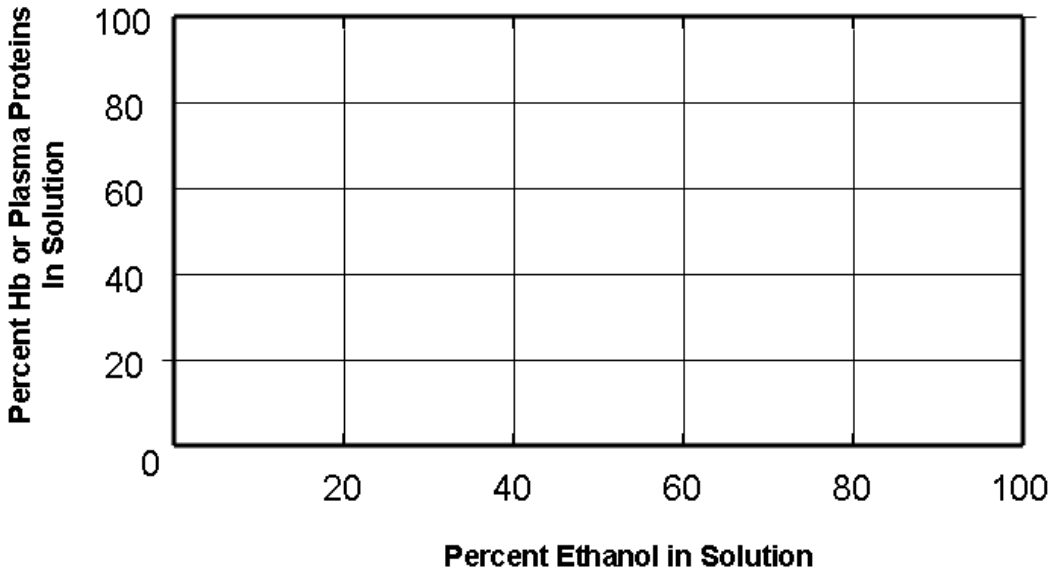
	Red	Purple	Brown	Basis for prediction
(1) Freshly drawn blood sample	X			Oxyhemoglobin in blood is red
Seal and store solution 1 for several hours.				
Add equal volume of ether to solution 1.				
Add $K_3Fe(CN)_6$ to solution 1.				
Add HCl to solution 1.				
Add CO to solution 1.				
Add $Na_2S_2O_4$ (dithionite) to solution 1.				

a. (6 pts) In the empty boxes above, put an "X" in the column that corresponds to the color you predict would result from the indicated treatment.

b. (9 pts) In the empty boxes in the last column, write the basis for each prediction.

c. (2 bonus points) What is the purpose of drawing blood in the presence of citrate or heparin?

2. (15 Points) The following two questions relate to the Zinoffsky (1886) article.
   a. (8 pts) Zinoffsky initially took extra time and effort to separate red blood cells from blood plasma, but later he simply avoided the 2% NaCl wash, added back distilled water, and proceeded to the first alcohol crystallization step. Based on Zinoffsky's comments, draw and label **<u>two</u>** graphs in the space below, one that represents the solubility of hemoglobin (Hb) and one that represents the solubility of serum proteins as a function of ethanol concentration in water.



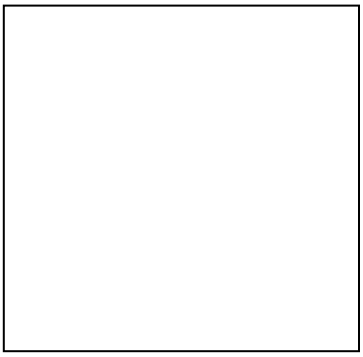
   b. (7 pts) Knowing what we do about hemoglobin now, it would be quite unlikely for the sulfur-iron stoichiometry for hemoglobin to be 1:4. Explain why this is so in words and illustrate with a drawing.

If you feel you cannot answer one of the following three 15-point questions relating to the jigsaw articles, consider Question #6 worth 10 points to substitute for question 3, 4, or 5.

3. (15 Points) The following two questions refer to the Digg et al (1933) and the Herrick (1910) articles.

   a. (8 points) Although they didn't know it, Diggs and coworkers estimated the genetic frequency of the sickle gene in the US black population. At that time, they and others did not appreciate the genetic relationship between sickle cell anemia and sickle cell trait. Had they known that, they could have applied the Hardy-Weinberg Law to their data and estimated the frequency of sickle cell anemia from the frequency of sickle cell trait. The Hardy-Weinberg Equation predicts the frequency of different genotypes based on allele frequencies and has the form $(p + q)^2 = p^2 + 2pq + q^2$, for two alleles. This relationship can be displayed visually as a Punnet Square in which each side has length $p + q$, and the areas within the square correspond to each term in the expanded equation.

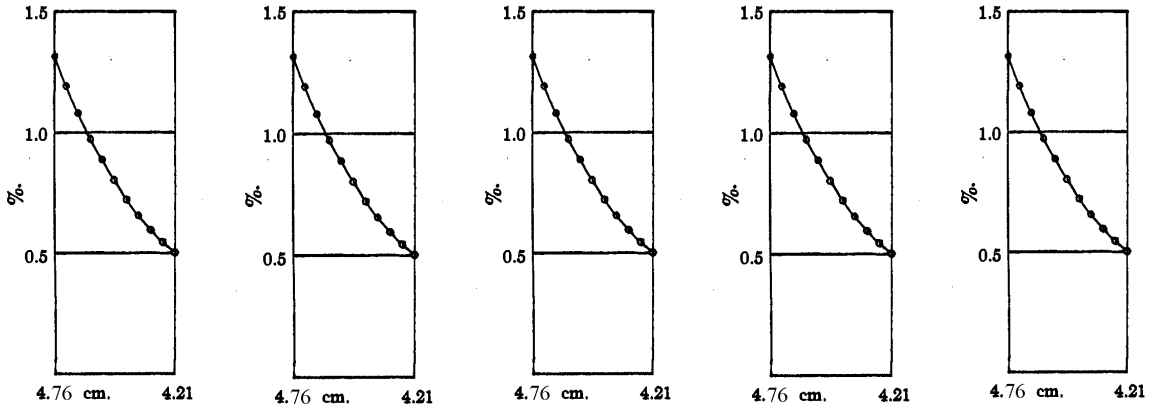
   In parts of Africa the frequency of the sickle cell gene can be as high as 40%. Fill in and label the diagram below. For such a population, identify the area in the diagram that would represent people with sickle cell anemia. Estimate the percentage of the population that would suffer from sickle cell sickle cell disease.



   b. (7 points) Herrick noted that his patient had a "tinge of yellow in the sclerae" and the urine "had a trace of bile." These related observations have significance in relation to the biochemistry of sickle cell disease. What is the connection between the sickle cell phenomenon and these clinical symptoms?

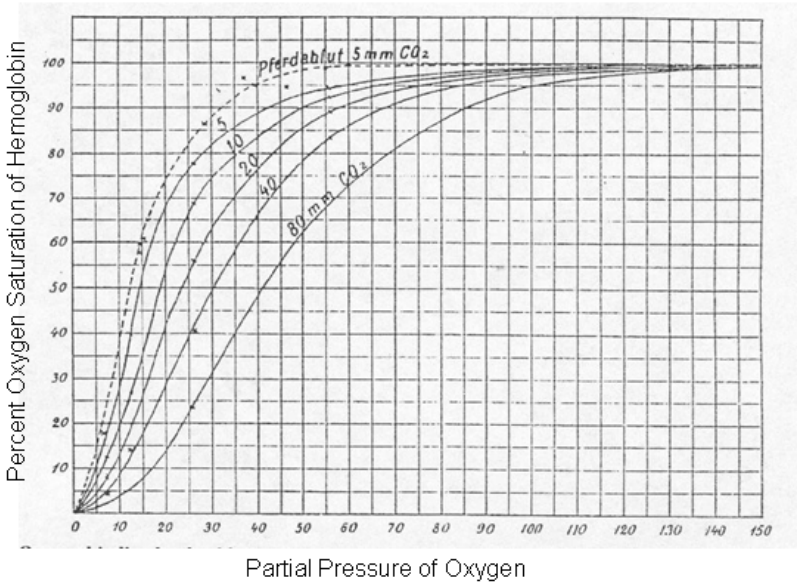
4. (15 points) Figure 7 from the Svedberg and Fåhraeus (1926) article is reproduced five times below. If conditions in the ultracentrifuge or the properties of hemoglobin were different, the concentration profile in Figure 7 might have been different. This question asks you to sketch in the concentration profile expected for five different hypothetical situations. In all cases except "e", the initial hemoglobin concentration in mg/ml is the same. Each answer is worth 3 points.
   a. Human CO hemoglobin rather than horse CO hemoglobin was used.
   b. The angular velocity, ω, of the centrifuge was doubled.
   c. The solvent was 10% ethanol in water rather than water.
   d. The concentration profile at 4 hours, rather than 30 hours.
   e. Hematin was used at the same molar concentration, rather than hemoglobin

a. b. c. d. e.



If you wish to explain your thinking, please use the space below.

5. (15 Points) The figure below shows the results of Bohr, Hasselbalch, and Krogh (1904) that appear in many current textbooks.



a. (4 pts) Put an "X" on the figure at a place that would correspond to the conditions that Peters (1912) used in his determination of the Specific Oxygen Capacity of hemoglobin.

b. (6 pts) Draw and label three vertical lines that would correspond respectively to the oxygen partial pressures in air at sea level, the lungs, and peripheral tissues.

c. (5 points) Describe the physiological significance of hemoglobin's sigmoid oxygen-binding curve and the effect of carbon dioxide on it.

d. (5 Bonus points) The arterial blood of a typical college student contains about 16g of HbO_2 per 100ml. **Estimate** how many ml of O_2 per 100ml of blood that represents at standard temperature and pressure? (Note: Estimation does not require a calculator. Any answer within a factor of 2 is correct. Show work on back of this page for credit.)

6. (10 points) **Only** answer this question if you have not answered one of the three preceding questions. Consider Question 3, 4, or 5 that you have not answered. Think about what information, concepts, or understanding you would needed to have had in order to have given a good answer. Based on that reflection, generate a list of five learning issues that would direct your study in pursuit of that goal.

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(12 Points each) *Defend* or *refute* **two** of the following five propositions with a short essay. Include diagrams to help communicate your answer where it is appropriate. Evaluation of your answers will be based on logical development of arguments that support your positions. Your arguments need to be based on material from this course, but they certainly can include other knowledge you may have.

7. The fact that sickle-cell anemia was not recognized by the medical profession before Herrick's 1910 article is a clear example of racial discrimination and health care disparity. Even in Herrick's article there are indications of racial prejudice.
8. There is no such thing as certainty in science because ideas are always tentative and subject to revision.

In addition to being a noted scientist and author of one of the jigsaw papers from last year, James Bryant Conant was president of Harvard University, an advisor to presidents, and a person deeply concerned with science education. In his book *On Understanding Science*, he lists the following three Principles of the "Tactics and Strategy of Science":

9. "*New concepts evolve from experiments or observations and are fruitful of new experiments or observations"*,
10. *"Significant observations are the result of 'controlled experiments' or observations; the difficulties of experimentation must not be overlooked*, and
11. *"New techniques arise as a result of experimentation and influence further experimentation.*"

Select one of these principles and defend or refute it with examples from our first several papers.