CHEM-342 Introduction to Biochemistry Name ______________________________
Midterm Examination - Individual Part (75%)
Wednesday, 23 March 2011
H. B. White – Instructor

Range 22-109/115 Ave ± SD = 79.7(69.3%) ± 17.7

Important - Please read this before you turn the page.

Write your name on every page.

There are 8 pages and 13 questions to this examination including this page.

Answer any 4, but only 4, of the first 8 questions.

This individual part of the midterm examination is worth 115 points.

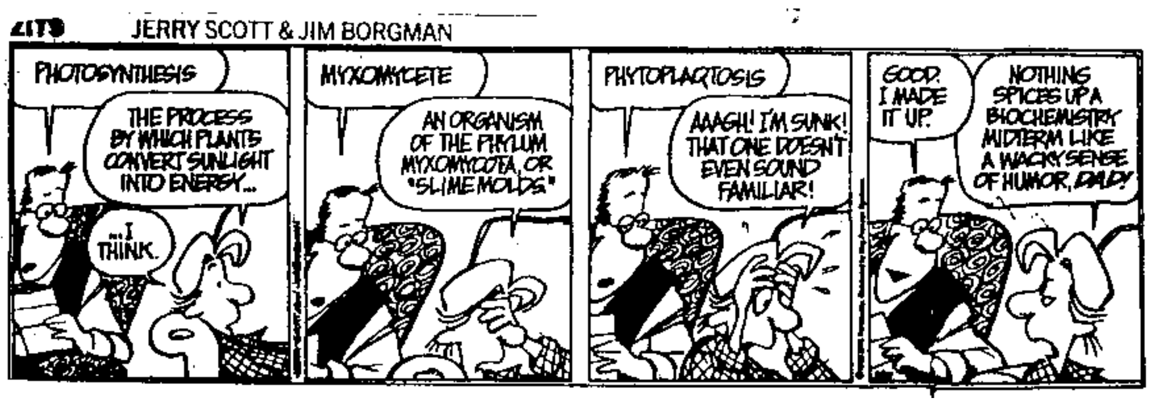
The examination is closed book until 8:15 AM. Thereafter you may refer to your notes, course reader, handouts, or graded homework assignments. Textbooks and reference books cannot be used. The examination ends promptly at 9AM.

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, 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. Also, **USE YOUR OWN WORDS**, transcription of words from your notes does not show me that you understand.



Part I Jigsaw Articles (60 points total)

The following eight questions relate to the jigsaw articles we have discussed in the past two weeks, one question for each article. Please answer only *four* of the eight. It is important that you include relevant and accurate images, equations, diagrams, and/or models in your answers to receive full credit. Each answer is worth up to 15 points.

1. Using information from the **Diggs et al. (1933)** article, develop a well-argued case that they had the information necessary to deduce that sickle cell anemia was a recessive genetic disease ***and*** that it was associated with hemoglobin.

2. **Herrick (1910)** noted that his patient had yellow sclerae which we now know is a consequence of red blood cell destruction and hemoglobin breakdown. What is the connection?

3. **Peters (1912)** used a different method for the titrimetric determination of iron than was used by Zinoffsky because he was concerned that chloride interferes with the iron determination based on permanganate. As an indicator, he included potassium thiocyanate (sulphocyanide). Describe the chemistry of Peters' determination of iron.

4. **Bohr et al. (1904)** observed a sigmoid relationship between the partial pressure of molecular oxygen and its binding to hemoglobin as well as the effect of bicarbonate in shifting the curves they obtained. How are the responses of hemoglobin to molecular oxygen and bicarbonate concentrations relevant to what happens in our body?

5. **Conant (1923)** says that the potential he measures for a mixture of hemoglobin and methemoglobin will change if carbon monoxide is introduced into his sealed electrochemical cell. Using the Nernst equation, show how this change in measured potential occurs when carbon monoxide is not being oxidized or reduced.

6. Functional Magnetic Resonance Imaging (fMRI) enables researchers to detect which parts of the brain are active. This is dependent upon changes in the magnetic moment of hemoglobin elucidated by **Pauling and Coryell (1936)**. What does this suggest is happening in the active regions of the brain?

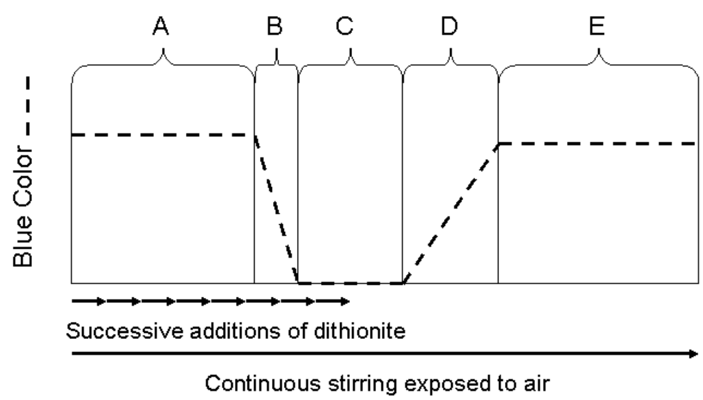
7. **Svedberg and Fåhareus (1926)** introduced the method of sedimentation equilibrium to determine the molecular weight of proteins in solution. Describe in pictures and words what sedimentation equilibrium means.

8. **Adair (1925)** actually determined the correct molecular weight of hemoglobin before Svedberg and Fahareus using osmotic pressure as a method. Others had tried this method for years and obtained inaccurate values. What makes osmometry so difficult and how did Adair deal with this problem?

Part II (Stokes and Zinoffsky)

9. (10 Points) If, as we now know, hemoglobin was not converted to methemoglobin in Stokes' experiments, then the coloring matter of blood was not being oxidized as Stokes thought. What was being reduced by $SnCl_2$ and $FeSO_4$ in Stokes' experiments? Show with a chemical equation how his experiment resulted in a color change in hemoglobin.

10. (10 Points) In the titration for the "blue" part of the "Blue and Gold" demonstration in class, the white powder ($Na_2S_2O_4$, sodium hydrosulfite, also known as sodium dithionite) was added to a solution of indigo. The figure below represents the progressive color changes and when they occurred.



Draw a line on the diagram that represents the concentration of oxygen though A-E regions of the diagram. Assume that the solution is saturated with oxygen at the start and assign it some value to use as a reference.

11. (15 Points total) The articles on hemoglobin by both Peters and Zinoffsky deal with stoichiometric relationships of iron to other elements. Peters showed that O_2 binds to hemoglobin specifically and stoichiometrically with iron. The 1:1 ratio of O_2 to Fe remains the same regardless of the animal source of the hemoglobin. Zinoffsky found a 2:1 stoichiometry of sulfur to iron in horse hemoglobin, a ratio that we can confirm from the now known complete three-dimensional, covalent structure of horse hemoglobin. In contrast to O_2:Fe, however, the minimum S:Fe stoichiometry can vary among hemoglobins from different species as is revealed in the table below. In all cases the percent iron by weight is close to 0.34%.

Stoichiometry of sulfur and molecular oxygen to iron in different hemoglobins.

	Animal Source of Hemoglobin				
	Horse	**Cow**	**Dog**	**Human**	**Chicken**
O_2:Fe	**1:1**	**1:1**	**1:1**	**1:1**	**1:1**
S:Fe	**2:1**	**5:2**	**5:2**	**3:1**	**9:2**

a. (9 points) If Zinoffsky had studied hemoglobin from the cow, rather than the horse, how would it have changed his conclusions?

b. (6 points) Given what you have learned about hemoglobin from textbooks, how is it possible for the S:Fe stoichiometry to vary among hemoglobins from different species while the O_2:Fe stoichiometry is constant?

12. (10 Points) Explain (1) why crystallization is a chemical criterion for purity and (2) why the elemental analysis of the mother liquor in Zinoffsky's study provided an additional indication that his hemoglobin crystals were pure. Feel free to use illustrations to support your explanations.

Part III Essay

13. (10 Points) The following two quotations were discussed in class on March 11. What point do these two cryptic statements try to make?

"H_2O is not 'water'." **Brian Coppola**

"For that matter, neither is 'water'" **H. B. White**

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