Introduction to Biochemistry
Final Examination - Individual (Part I)
Thursday, 28 May 2009
7:00 – 8:45 PM
H. B. White – Instructor

Your Name_____

"Ability is what you're capable of doing.
Motivation determines what you do.
Attitude determines how well you do it."

Lou Holtz

90 Points

Important - Please read this before you turn the page.

- For the first hour, this is a closed-book examination. From 8 – 8:45 PM you may refer to your course notes and materials.
- 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. Among the "right answers" I will read, some will be better than others because they show greater depth of understanding, avoid extraneous or inaccurate information, provide a more logical structure, use appropriate examples, and choose words with precision. Better quality answers will receive higher marks. Therefore organize your thoughts before you write or draw. 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.
- This examination emphasizes work done in this course since Spring Break; however, knowledge is not so conveniently compartmentalized. Therefore, you should feel free to use any relevant example from your experience, if it is appropriate.
- There are 9 pages to this part of the examination (counting this cover page.). Please write your name on each page. Feel free to use the backs of pages, if you need more space.
- Part I (90 points) This individual part of the examination, includes 10 problems and essay questions.
- Part II (30 points) The group part of the examination will require you to deal with new information collaboratively.
- If you complete Part I early, you may leave the room and move to 205 Brown Lab where the Group Part of the examination will begin about 8:50 PM.
- You may refer to your notes, course reader, handouts, or graded homework assignments after the first hour of the examination and for the group part of the examination.
- Attempt to draw a picture or diagram as part of your answer to every question.
- Have a productive and safe summer.

I. Seminars and Visitor Talks	15 points
II. Problems	60 points
III. Essay	15 points

I. **Seminars and Visitor Talks**: (5 points each, 15 points total): The following require brief but well-worded answers that concisely and accurately state what you want to say.

1. You were asked to attend two seminars during the last half of the semester. Pick one and describe something about it even though it may have been pretty advanced.

2. Dr. Howard Dintzis personally knew Linus Pauling, Vernon Ingram, Max Perutz, Francis Crick, and many other prominent scientists of the past century of whom he talked about during his visit to the class on May 6. He also discussed some of the circumstances relating to his classic experiment that we discussed in class. Write a short paragraph about one or two things that Dr. Dintzis talked about that you found interesting.

3. Dr. Carlton Cooper, a UD Biology faculty member who is heterozygous for the sickle cell gene, spoke to the class on May 15. How did Dr. Cooper discover he had sickle cell trait?

II. Problems (60 Points total)

4. (10 Points) Eighteen percent of a community in Africa has sickle cell trait.
   A. (5 Points) What percent of the children born in this community would be expected to have sickle cell disease?

   B. (5 Points) Assuming that none of the people with sickle cell disease reproduce and that the frequency of the sickle cell gene in this population is being maintained at a constant level by the reduced reproduction due to malaria among people who lack the sickle cell gene, estimate the reproductive cost of malaria in this community. Express this quantitatively.

5. (10 Points) Carbon monoxide is deadly because it can bind to hemoglobin and competitively displace oxygen. In 1906, Gustav Mann wrote on page 498 of his book, "Chemistry of the Proteids,"

> *Identification* [of carbonmonoxyhemoglobin] *by the spectroscope is not easy, as the absorption bands closely resemble those of oxyhemoglobin, but two methods allow of its ready recognition, namely: firstly, the addition of ammonium sulfide or Stokes' reagent* [Ferrous tartrate] *which produces no change, while in the case of oxyhemoglobin they convert the later into reduced hemoglobin with its characteristic spectrum.....*

Why does Stokes' reagent cause a spectral change with oxyhemoglobin and not with carbonmonoxyhemoglobin? Convert Mann's statement to representations of chemical reactions.

6. (10 Points) Isotopic tracers have proved very useful in biochemical experiments. The articles by Shemin and Rittenberg (1946) and by Dintzis (1961) used isotopes.

   A. (2 Points) What isotopic tracer(s) did each use?

      Shemin and Rittenberg (1946)

      Dintzis (1961)

   B. (5 Points) Describe how each of these isotopes differs from its corresponding common isotope.

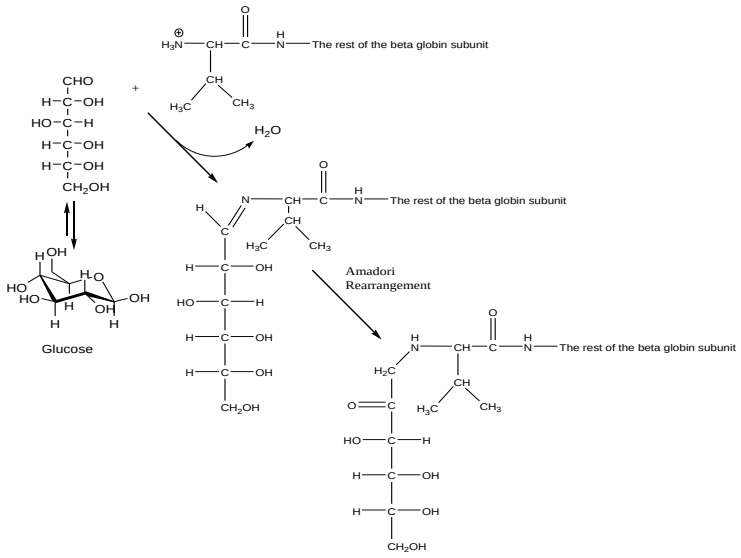
   C. (3 Points) What analytical techniques were used in each case to detect the isotopes?

      Shemin and Rittenberg (1946)

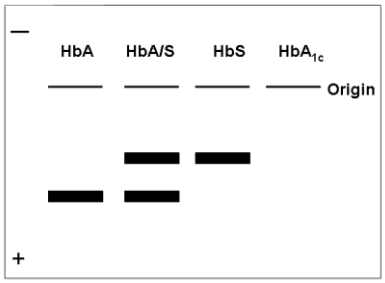
      Dintzis (1961)

7. (10 Points) Dr. Cooper mentioned Hemoglobin A_{1c}. This is HbA that has been covalently modified with a molecule of glucose. Virtually everyone has HbA_{1c} to some extent. The amount of HbA_{1c} in one's blood is a time-averaged indicator of glucose levels in a person's blood. Thus, it can be used to diagnose Type II diabetes and also to determine how well a diabetic is controlling blood sugar over the three-month life-span of red blood cells. If the percentage is greater than 7.0%, treatment is indicated.

   HbA_{1c} forms when the amino terminal valine of the β-chain of hemoglobin reacts non-enzymatically with the open-chain aldehyde of glucose and undergoes an Amadori Rearrangement (See below). This covalently and irreversibly attaches the glucose to hemoglobin. Being concentration dependent, the higher the glucose levels, the more HbA_{1c} is formed. It is removed when the red blood cells are destroyed after three months.

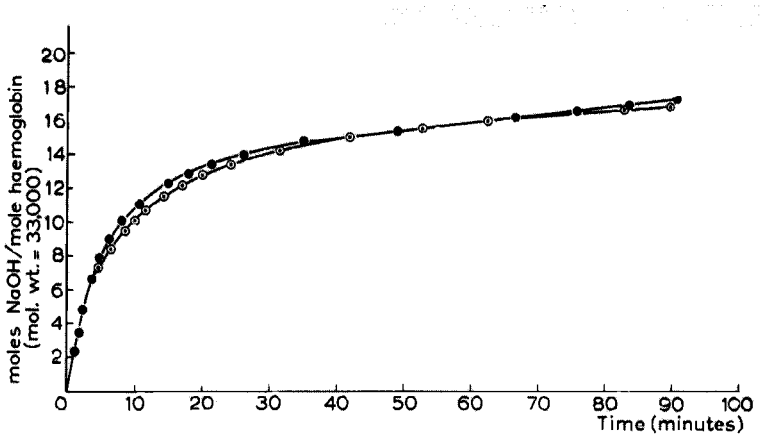


   A. (5 Points) On the diagram below depicting the electrophoretic patterns for HbA, HbAS, and HbS at pH = 7, predict the location of HbA_{1c}. Explain your reasoning.



   B. (5 Points) The amino acid replacement in HbS occurs in the amino-terminal tryptic peptide of the β-chain, the same peptide that is glycosylated. If Ingram were trying to sequence the HbA_{1c} or HbS_{1c} tryptic peptide, what problems would he have encountered with his methodology?

8. (10 Points) A group of CHEM-342 students and their tutor were beginning to discuss the Ingram (1958) article and were trying to interpret his Figure 1 shown below.



Bill – *I have no idea what this graph shows. Why is the molecular weight for hemoglobin 33,000 and not 66,000? Why is NaOH being used to titrate hemoglobin? Where is the acid coming from anyway?*

Jill – *My understanding is that it counts the number of peptide bonds in hemoglobin cleaved by trypsin. In other words, there were about 18 bonds broken and 18 protons released in an hour and a half.*

Tutor Phil – *Fine, but there are more than 18 spots on Ingram's peptide map. How do you explain that, if only 18 peptide bonds were hydrolyzed?*

Will – *You guys are all hung up on stoichiometry. All Ingram wants to know is when the reaction is complete. The number of moles of NaOH is irrelevant. It depends on the pH of the reaction.*

Help out these students. Where are the protons coming from in Ingram's experiment? Why are there more peptides produced than protons? Illustrate your answer with chemical reactions.

9. (10 Points) Iron is an essential dietary mineral. As a typical adult human, you have about 2 grams of iron in your body of which about 70% is associated with the heme group in hemoglobin. Knowing what you do about the structure and biological lifetime of a hemoglobin molecule, estimate to within one order of magnitude (correct within a factor of plus or minus 10), how many molecules of tetrameric hemoglobin your body will make during this exam?

III Essay

10. (15 Points) Being a biochemistry major suggests that you have an interest in biology and chemistry but prefer to think about biological problems in molecular and mechanistic terms. The articles you have read range from quite biological to the more chemical. Select three examples from our readings this semester and discuss the biological significance of the chemical results in each.