Important - Please read this before you turn the page.

- Write your names or group number on each page of the exam you turn in.
- You may refer to your notes, course reader, handouts, or graded homework assignments. (Wireless laptop computers and textbooks cannot be used.)
- Please read each question carefully and make sure that you have thought it through with everyone’s input before converging on a solution.
- If you do not agree with your group, you may submit the examination under your own name for separate grading.
1. In 1946, Shemin and Rittenberg discovered by accident that glycine was a direct precursor of the heme group of hemoglobin. Shemin was actually interested in the synthesis and turnover of proteins. The simplest amino acid he could enrich with $^{15}$N was glycine. He consumed a total of 66 g of the labeled glycine at hourly intervals for almost 3 days. Then he removed samples of his own blood periodically for more than 7 months and had the globin and heme separately analyzed for incorporation of $^{15}$N. In related study, he analyzed stercobilin, an excreted product of heme (hemin) breakdown related to bilirubin, as shown below.

![Graph showing $^{15}$N concentration in heme and stercobilin](image)

From J. Biol. Chem, 184, 351 (1950)

Fig. 1. $^{15}$N concentration in heme and stercobilin of a normal man after the start of feeding $^{15}$N-labeled glycine for 2 days.

Some of the conclusions from Shemin’s experiments are:

i. Glycine is a biosynthetic precursor for heme.

ii. Most of the red blood cells have a mean life span of about 127 days.

iii. Heme is not reutilized for synthesis of hemoglobin

![Graph showing time vs. $^{15}$N concentration](image)

From J. Biol. Chem, 166, 627 (1946)

a. (9 points) Based on the information in Shemin & Rittenberg (1946) and information you have gained from other sources, construct a model (draw a diagram) of the
relationship of heme, globin, and stercobilin to glycine as revealed by pulse-case experiments with $^{15}$N from glycine.

b. (8 points) Explain how it is possible for the atom percent $^{15}$N in stercobilin between 110 and 140 days is greater that it ever was in heme isolated from hemoglobin.
c. (8 points) Shemin and coworkers repeated their study on a person who had sickle cell anemia with the results shown at the right. Qualitatively and quantitatively, how does this figure differ from normal? What can you conclude? How would your model for part “a” be modified to reflect these data?

2. Bonus (5 points) Close to 1.0% of the weight of an average adult human is hemoglobin. Assuming you and the other members of your group are typical, estimate to within an order of magnitude the number of hemoglobin molecules your group will synthesize during this examination.