

Name \_\_\_\_\_

Student number \_\_\_\_\_

**University of Guelph**  
**Department of Chemistry and Biochemistry**  
**19-356**  
**Structure and Function In Biochemistry**

**Midterm Test, March 3, 1998.**

**Time allowed, 90 min.**

Answer questions 1-20 on the computer scoring sheet provided.

Only one option is correct for each of these questions.

Use pencil to fill in the circles representing your chosen answer; and erase cleanly if you make an error. Do not use ink or white-out on the computer scoring sheet.

You may mark your answer on the question paper for your own records, however in case of a discrepancy between question paper and the computer scoring sheet, the choice shown on the computer sheet will be taken as final.

Answer questions 21-24 directly on the question paper.

Questions 1-20 have a weight of 1 mark each

Questions 21-24 have marks as indicated

20 marks

20 marks

=====

40 marks

total

Q.21-22	Q.23	Q. 24	subtotal
9	7	4	20

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Answer questions 1-20 on the computer scoring sheet.

Value 1 mark each

1. **Thalassemia with two b-globin genes defective is not always lethal because:**  
A)  $\alpha$  hemoglobin functions adequately on its own.  
B) The other  $\beta$  globin genes make adequate supplies of hemoglobin.  
C) Fetal  $\gamma$ -globins may continue to be expressed in adult life.  
D) The body makes do with myoglobin provided no strenuous activity is undertaken.  
E) This condition is never observed. 1) A B C D E
  
2. **The Bohr effect is the reduced affinity of hemoglobin for  $O_2$**   
A) Due to binding of 2,3-bisphosphoglycerate  
B) Due to high altitude.  
C) Due to lower pH  
D) In fetal hemoglobin.  
E) Resulting from the hemoglobin S mutation. 2) A B C D E
  
3. **ATP acts on aspartate transcarbamoylase:**  
A) By providing energy for the reaction.  
B) By phosphorylating the substrate.  
C) As a homotropic effector  
D) As a feedback inhibitor.  
E) By binding and stabilizing the R state of the enzyme. 3) A B C D E
  
4. **Vitamin K is required for normal blood clotting because:**  
A) Vitamin K binds to thrombin making it more active.  
B) Vitamins make you more healthy.  
C) Vitamin K is required for formation of  $\gamma$ -carboxyglutamate in the active site of thrombin.  
D) Vitamin K is required for formation of  $\gamma$ -carboxyglutamate in prothrombin.  
E) Vitamin K binds  $Ca^{2+}$  to neutralize the negative charge of fibrinogen. 4) A B C D E
  
5. **Which of the following does not increase activity in the cyclic AMP-protein kinase cascade?**  
A) Adenylate cyclase  
B) Protein kinase A  
C) Glycogen Synthase  
D) Phosphorylase kinase  
E) Phosphorylase 5) A B C D E
  
6. **Caffeine acts as a stimulant by:**  
A) Increasing synthesis of cyclic AMP  
B) Stimulating G-protein to bind GTP  
C) Preventing breakdown of cyclic AMP  
D) Binding to protein kinase A.  
E) Binding to a hormone receptor on the cell surface. 6) A B C D E
  
7. **The initial activation of trypsinogen requires:**  
A) Enteropeptidase  
B) Pepsinogen  
C) Chymotrypsinogen  
D) Chymotrypsin  
E) Pancreatic trypsin inhibitor. 7) A B C D E

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8. **Which statement about 2,3- bisphosphoglycerate (BPG) is untrue?**  
A) People who live at high altitude have higher BPG levels to enhance O<sub>2</sub> release in tissues.  
B) BPG binds to a positively charged region between the β -globin subunits.  
C) BPG binds more weakly to fetal hemoglobin, so O<sub>2</sub> binding is stronger.  
D) BPG binding favours the R state of hemoglobin.  
E) BPG is derived from intermediates of the glycolysis pathway. 8) A B C D E
9. **In the Monod-Wyman-Changeux model of allosteric cooperative binding, e.g. of O<sub>2</sub> by hemoglobin, which one of the following is assumed?**  
A) That all subunits change from T to R together.  
B) Each subunit changes from T to R as it binds O<sub>2</sub>.  
C) All subunits bind O<sub>2</sub> simultaneously.  
D) high affinity sites are occupied first.  
E) O<sub>2</sub> can't bind until hemoglobin is in the R state. 9) A B C D E
10. **Which statement about Histidine F8 in the globin sequence is incorrect:**  
A) changes position in the R state to T state transition  
B) is the 5th ligand for Fe<sup>2+</sup>. C) forces the 6th ligand into a "bent" configuration.  
D) pulls Fe<sup>2+</sup> out of the heme plane. E) is found in myoglobin and all hemoglobins.  
10) A B C D E
11. Plots of O<sub>2</sub> binding by myoglobin (Mb) are made in terms of fractional occupancy θ.  
**Which formula correctly represents Y?**  
A)  $\theta = \frac{[MbO_2]}{[Mb]+[MbO_2]}$  B)  $\theta = \frac{[Mb]}{[MbO_2]}$  C)  $\theta = \frac{[MbO_2]}{[Mb]}$   
D)  $\theta = \frac{[Mb]+[MbO_2]}{[MbO_2]}$  E)  $\theta = \frac{[MbO_2]}{[Mb][O_2]}$  11) A B C D E
12. Which of the following correctly completes the statement  
**Binding of aspartate by ATCase is a sigmoidal function of [aspartate] because**  
A) Aspartate molecules bind to all catalytic subunits simultaneously.  
B) As each aspartate binds, it changes the c-subunit it's bound to into the R-state.  
C) Aspartate is a positive heterotropic effector for ATCase.  
D) Each aspartate bound increases the probability that the whole c<sub>6</sub>r<sub>6</sub> will convert to the R state.  
E) Binding negatively charged aspartate favours the T-state. 12) A B C D E
13. **Which of the following is not a serine protease?**  
A) Factor XIIa B) Fibrin C) Plasmin  
D) Thrombin E) Tissue Plasminogen Activator 13) A B C D E



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21. Factor XIIIa plays a unique role in the blood clotting system.

i) Which serine protease activates factor XIII to give to XIIIa? \_\_\_\_\_

1 mark

ii) Once factor XIIIa is active, what reaction does it catalyze, and what effect does this have on the blood clot?

3 marks

22. Prothrombin and the zymogen forms of several serine protease blood clotting factors, e.g. factor X, have an unusually large propeptide which is important in the activation process.

What modified amino acid is found in this propeptide? \_\_\_\_\_

1 mark

How does this modified amino acid participate in the activation mechanism?

Explain why blood clots in contact with glass, which has a negatively charged surface.

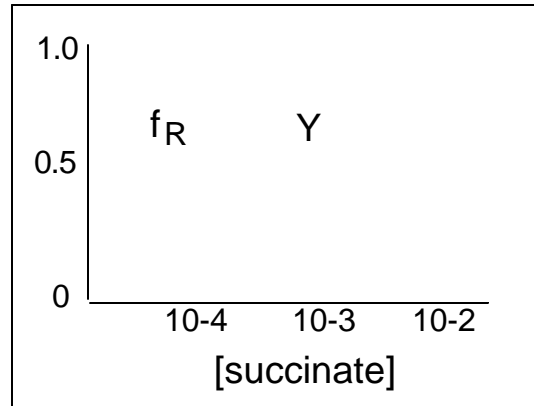
What natural negatively charged surface triggers blood clotting in the body?

4 marks

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23. The diagram on the right shows a plot of  $f_R$ , the fraction of ATCase molecules in the R allosteric state, as a function of [succinate]. Also plotted is Y, the fraction of substrate sites occupied by succinate.



What instrumental method was used to measure  $f_R$ ?

\_\_\_\_\_

1 mark

What property of ATCase changes on adopting R state to allow this measurement?

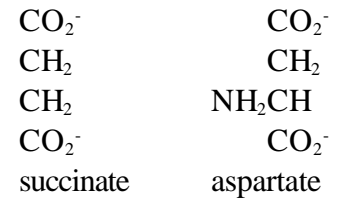
\_\_\_\_\_  
\_\_\_\_\_

1 mark

Why was the experiment done with succinate instead of aspartate, the natural substrate?

\_\_\_\_\_  
\_\_\_\_\_

1 mark



What is the significance of the fact that the curve for  $f_R$  lies to the left of the curve for occupancy, Y?  
What conclusion might be drawn if the two curves were superimposed?

3 marks.

Aspartate is one substrate for aspartate transcarbamoylase (ATCase); name the other:

\_\_\_\_\_

1 mark

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24. The arrangement of subunits in hemoglobin is best described in terms of two globin pairs,  $\alpha_1\beta_1$  and  $\alpha_2\beta_2$  (subscripts identify different subunits rather than showing stoichiometry).

What structural changes are noted in the change from T to R state of hemoglobin?

How is the orientation of  $\alpha_1\beta_1$  to  $\alpha_2\beta_2$  changed? \_\_\_\_\_

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1 mark

Which combination is least affected by change from T to R?

$\alpha_1\beta_1$        $\alpha_1\beta_2$        $\alpha_1\alpha_2$        $\beta_1\beta_2$       (circle one)

Which combination alters its hydrogen bonding pattern on change T to R?

$\alpha_1\beta_1$        $\alpha_1\beta_2$        $\alpha_1\alpha_2$        $\beta_1\beta_2$       (circle one)

Which combination moves further apart on change T to R?

$\alpha_1\beta_1$        $\alpha_1\beta_2$        $\alpha_1\alpha_2$        $\beta_1\beta_2$       (circle one)

Which combination moves closest together on change T to R?

$\alpha_1\beta_1$        $\alpha_1\beta_2$        $\alpha_1\alpha_2$        $\beta_1\beta_2$       (circle one)

Which combination contains the 2,3-bisphosphoglycerate binding site?

$\alpha_1\beta_1$        $\alpha_1\beta_2$        $\alpha_1\alpha_2$        $\beta_1\beta_2$       (circle one)

Which combination contains salt bridges that help restore the molecule to the T state?

$\alpha_1\beta_1$        $\alpha_1\beta_2$        $\alpha_1\alpha_2$        $\beta_1\beta_2$       (circle one)

3 marks