

Name _____

Student number _____

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

Midterm Test, March 6, 1997.

Time allowed, 120 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 21-25 directly on the question paper.

Questions 1-20 have a weight of 1 mark each

20 marks

Questions 21-25 have marks as indicated

20 marks

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40 marks total

Q.21-22	Q. 23-24	Q.25	subtotal
_____	_____	_____	_____
7	7	6	20

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Answer questions 1-20 on the computer scoring sheet.

Value 1 mark each

1. Identify the correct completion of the statement:

Heme-Fe²⁺ complex in solution

- A) can't bind O₂.
 B) is easily oxidized to Fe³⁺ by O₂.
 C) binds H₂O with high affinity.
 D) binds CO₂ more tightly than O₂.
 E) is a good transporter for O₂.

1) A B C D E

2. Identify the correct completion of the statement:

In the globin sequence, Histidine E7

- A) replaces glutamate (E) at position 7 of the polypeptide.
 B) is the 5th ligand for Fe²⁺.
 C) forces the 6th ligand into a "bent" configuration.
 D) pulls Fe²⁺ out of the heme plane.
 E) is present in myoglobin but not hemoglobin.

2) A B C D E

3. **Structure of globins is 70% α -helix because**

- A) the polypeptide lacks amino acids that prefer β -sheet.
 B) amino acids that prefer β -sheet are scattered at random, but α -helical amino acids are organized in clusters.
 C) α -helical amino acids face outwards but β -sheet amino acids face inwards.
 D) α -helical amino acids face inwards but β -sheet amino acids face outwards.
 E) myoglobin and α -globin are α -helix but β -globin is β -sheet.

3) A B C D E

4. **Which hemoglobin combination would be unexpected in a fetus 7½ months before birth?**

- A) $\alpha_2\varepsilon_2$ B) $\alpha_2\gamma_2$ C) $\zeta_2\varepsilon_2$ D) $\zeta_2\gamma_2$ E) $\zeta_2\beta_2$ 4) A B C D E

5. Plots of O₂ binding by myoglobin are made in terms of fractional occupancy **q**.**Which formula correctly represents q**

- A) $q = \frac{[MbO_2]}{[Mb] + [MbO_2]}$ B) $q = \frac{[Mb]}{[MbO_2]}$ C) $q = \frac{[MbO_2]}{[Mb]}$
 D) $q = \frac{[Mb] + [MbO_2]}{[MbO_2]}$ E) $q = \frac{[MbO_2]}{[Mb][O_2]}$ 5) A B C D E

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6. **Binding of O₂ by hemoglobin is a sigmoidal function of pO_2 because**
- A) Four O₂ molecules bind to each hemoglobin simultaneously.
 - B) β -globin has lower O₂ affinity than α -globin.
 - C) β -globin has higher O₂ affinity than α -globin.
 - D) hemoglobin has lower O₂ affinity than myoglobin.
 - E) the binding affinity of hemoglobin subunits increases as each O₂ is bound.
- 6) A B C D E
7. **In the Monod-Wyman-Changeux model of allosteric cooperative binding, e.g. of O₂ 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 O₂.
 - C) All subunits bind O₂ simultaneously.
 - D) high affinity sites are occupied first.
 - E) O₂ can't bind until hemoglobin is in the R state.
- 7) A B C D E
8. **Which of the following is not observed in the T to R transition of hemoglobin subunits?**
- A) The dimer pair $\alpha_1\beta_1$ rotates 15° relative to $\alpha_2\beta_2$
 - B) β_1 moves closer to β_2
 - C) Large structural changes take place in the contact between α_1 and β_1 globins.
 - D) New hydrogen bonds form in the interface between α_1 and β_2 globins.
 - E) Histidine F8 moves closer to the plane of the heme ring system.
- 8) A B C D E
9. **Which of the following statements is correct with regard to 2,3-bisphosphoglycerate?**
- A) Binding 2,3-bisphosphoglycerate increases binding of O₂ at a given pO_2 .
 - B) One mole of 2,3-bisphosphoglycerate binds per β -globin subunit.
 - C) 2,3-bisphosphoglycerate is a normal intermediate in the glycolysis pathway.
 - D) Binding of 2,3-bisphosphoglycerate favours the R state of hemoglobin.
 - E) 2,3-bisphosphoglycerate enhances O₂ release in the peripheral capillaries.
- 9) A B C D E
10. Individuals with α -thalassemia have small amounts of **β_4** hemoglobin.
Which of the following correctly describes a property of β_4 hemoglobin?
- A) β_4 hemoglobin can't bind O₂.
 - B) β_4 hemoglobin has a tendency to crystallize.
 - C) β_4 hemoglobin binds O₂ with low affinity.
 - D) The binding of O₂ by β_4 hemoglobin is more like myoglobin than normal hemoglobin.
 - E) β_4 hemoglobin is replaced by persistent expression of γ globin in adult life.
- 10) A B C D E

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11. **High [ATP] increases the rate of catalysis of aspartate transcarbamylase because**
 A) ATP is required in the catalytic process.
 B) ATP causes release of active c subunits.
 C) ATP hydrolysis provides energy for the reaction.
 D) ATP is a positive homotropic allosteric effector.
 E) ATP binding shifts the ATCase from the T to the R state. 11) A B C D E
12. **The sedimentation coefficient of ATCase decreases when phosphonylacetyl-L-aspartate (PALA) is added. This indicates that:**
 A) the ATCase molecule has increased in mass due to binding substrate analog.
 B) the ATCase molecule is more open, increasing its friction factor.
 C) the ATCase molecule has split up into smaller subunits.
 D) the ATCase molecule has closed, up making it appear smaller.
 E) the ATCase molecule has decreased in mass. 12) A B C D E
13. The c_6r_6 organization of ATCase is dissociated into smaller subunits by covalent binding of *p*-hydroxymercuribenzoate. **Which of the following is not true:**
 A) the c_3 component is catalytically active.
 B) the c_3 component is under allosteric control.
 C) the r_2 component can bind ATP or CTP.
 D) the r_2 and c_3 components recombine into fully functional allosterically regulated ATCase.
 E) a single c subunit can't bind substrate. 13) A B C D E
14. **Which of the following is not true for enzymes which display negative cooperativity?**
 A) Substrate binding affinity is reduced at high [S].
 B) Substrate binding affinity is enhanced at low [S].
 C) Allosteric effects are based on the sequential model of Koshland, Nemethy and Filmer.
 D) The binding or activity plot is sigmoidal.
 E) The binding energy for the first substrate molecule is higher than for the last substrate molecule. 14) A B C D E
15. **Which of the following statements is not true with regard to zymogen activation?**
 A) At low pH pepsinogen cleaves itself to remove a peptide that blocks the active site.
 B) Cleavage of chymotrypsinogen by trypsin removes a peptide that blocks the active site.
 C) Cleavage of chymotrypsinogen by trypsin introduces a new positively charged α -amino group at Ile 16 which helps position Asp 194 correctly.
 D) Self-cleavage of π -chymotrypsin to form α -chymotrypsin is not essential for activation.
 E) Cleavage of chymotrypsinogen by trypsin positions Ser 195 and Gly 193 correctly for substrate binding. 15) A B C D E

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16. **Which of the following statements best describes the working of natural protease inhibitors such as pancreatic trypsin inhibitor and α 1-antitrypsin?**
- A) Very strong binding of the inhibitor increases the activation energy for the protease reaction.
 - B) The inhibitors bind covalently to the protease.
 - C) Reactive groups in the inhibitor modify the protease irreversibly.
 - D) The inhibitors lack the key amino acid that is the target for the protease so can't be hydrolyzed.
 - E) The inhibitor is itself a protease that attacks and deactivates the target protease.
- 16) A B C D E
17. **Which of the following factors is not part of the intrinsic pathway for blood clotting?**
- A) Factor XII
 - B) Factor XI
 - C) Factor IX
 - D) Factor VIII
 - E) Factor VII
- 17) A B C D E
18. **Which of the following blood clotting factors is not a serine protease?**
- A) Factor XII
 - B) Factor XI
 - C) Factor IX
 - D) Factor VIII
 - E) Factor VII
- 18) A B C D E
19. **Which of the following substances is a positive allosteric effector of muscle phosphorylase *b*?**
- A) ATP
 - B) Glucose
 - C) Caffeine
 - D) cyclic AMP
 - E) AMP
- 19) A B C D E
20. **Dicoumarol in spoiled hay causes hemorrhagic disease in cattle. Which of the following statements is not true?**
- A) γ -carboxylation of prothrombin is blocked the presence of dicoumarol.
 - B) The abnormal prothrombin binds Ca^{2+} weakly.
 - C) Without bound Ca^{2+} , prothrombin can't be activated.
 - D) The Ca^{2+} binding sites are near the N-terminus of prothrombin.
 - E) Ca^{2+} binding is required for thrombin to bind its substrate, fibrinogen.
- 20) A B C D E

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21. i) Briefly explain why the **positive homotropic effect** gives a sigmoidal curve for an allosterically regulated enzyme such as ATCase.
- ii) sketch the sigmoidal curve for substrate only, then add two curves showing the effect of adding a) an allosteric effector which has a **positive heterotropic effect**, and b) an allosteric effector with a **negative heterotropic effect**. Label these curves **positive** and **negative**.

3 marks

22. **What amino acid change is found in the polypeptide sequences of Hemoglobin S?**

_____ in normal HbA at position ____ of ____ globin is replaced by _____

Why does this change lead to **aggregation of deoxyhemoglobin S** but **not the oxy form**?

4 marks

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

Name the **product** of the normal reaction _____

Briefly explain why it is useful to the organism that **ATP binding activates ATCase** while **CTP binding should inhibit** the reaction.

3 marks

24. Outline briefly how **cleavage of fibrinogen by thrombin** allows formation of a fibrin clot. What additional changes **convert the fibrin from soft clot to hard clot**? **What factor** is responsible for this change, and **how is it activated**?

4 marks

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25. Draw the sequence of steps in the **cascade for stimulation of muscle glycogen phosphorylase** activity by the **hormone epinephrine**.

3 marks

Draw the structures of 3',5'-cyclic AMP and ordinary 5'-AMP **showing how the phosphate is linked to the ribose in each case**; the adenine portion can be represented as Ade.

3',5'-cyclic AMP:

5'-AMP

2 marks

How does **caffeine** elevate the level of glucose in the blood?

1 mark