BIOC*3560 Winter 2008
Sample Midterm Examination
(From March 2007)

Warning: Topics covered may vary between semesters. Therefore, this midterm is best used as a guide for format and level of detail.

Check your exam paper carefully; you should have 12 different pages. Make sure your seven-digit student ID number is entered correctly in the space provided above and on the computer scoring sheet.

Answer Part I, questions 1-30, on the computer scoring sheet provided. Only one option is correct for each of these questions. Use **black lead pencil** to fill in the circles corresponding to your answer; erase cleanly if you make a mistake. **Do not use ink or white-out on the computer scoring sheet.**

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

Answer Part II, questions 1-9, directly on the question paper. **Answer only in ink (NOT red!) and only in the space provided**.

Part I 30 marks	
Part II 30 marks	
Total 60 marks	

<u>Part I</u>: MULTIPLE CHOICE QUESTIONS 1- 30 (*30 marks*)

For each question, please fill in the circle corresponding to the correct answer on the computer scoring sheet provided.

1. The oxygen-binding curve for myoglobin is best described as:
   (A) linear
   (B) logarithmic
   (C) sigmoidal
   (D) hyperbolic
   (E) complex

2. In oxygenated myoglobin, one of six coordination bonds involving the heme Fe^{2+} is formed with O_2 and another is formed with:
   (A) His E7
   (B) His F8
   (C) Tyr F8
   (D) Ser F8
   (E) His HC3

3. Which statement accurately describes the Bohr effect in hemoglobin-O_2 binding?
   (A) H^+ and CO_2 react with Hb, contributing to salt bridges that stabilize the T state
   (B) H^+ and CO_2 react with Hb, blocking salt bridge formation that stabilizes the T state
   (C) H^+ binds to amino termini
   (D) CO_2 binds to the central cavity
   (E) It explains what happened to Rex Grossman in the Superbowl

4. Which of the following statements regarding heme is true?
   (A) It has a higher affinity for O_2 than for CO
   (B) It binds oxygen allosterically
   (C) It contains 4 pyrrole rings, linked by methane bridges
   (D) It contains 4 pyrrole rings and a system of conjugated C=C bonds
   (E) It is encoded by several genes

5. If T (inactive) and R (active) are the two possible conformations for the six identical subunits of a hexameric allosteric enzyme, then according to the **concerted model**:

(A) Subunits can exist in the R form when not bound to substrate

(B) Enzyme saturated with substrate must be in the T_6 form

(C) Hybrid forms (e.g. R_3T_3) are found at some substrate concentrations.

(D) Allosteric activators shift the equilibrium towards the T_6 state.

(E) Allosteric inhibitors increase the proportion of enzyme in the R_6 form

6. In the analysis of hemoglobin-O_2 binding, P_{50} as used in the Hill equation is:

(A) The partial pressure of O_2 that saturates hemoglobin

(B) The partial pressure of O_2 that gives half-occupancy

(C) The partial pressure of O_2 that gives a Hill plot slope = 1.00

(D) The partial pressure of O_2 that inhibits cooperative ligand-binding

(E) The partial pressure of O_2 for maximal O_2 binding

8. You poison your roommates with Warfarin (a competitive inhibitor of vitamin K). They slowly bleed to death due to reduced blood clotting as a result of:

(A) Increased γ-carboxylation of factor X

(B) Reduced γ-carboxylation of factor X

(C) Increased γ–carboxylation of prothrombin

(D) Reduced γ–carboxylation of prothrombin

(E) Inhibition of a transglutaminase

9. Which of the following statements is **false** with respect to caspases:

(A) They do not regulate blood clotting

(B) They are synthesized in an inactive form

(C) They are cysteine proteases

(D) They cleave proteins after aspartate residues

(E) They contain Asp-His-Ser in their catalytic site

10. Non-reactive transition state analogues are useful in the study of enzymes because they:
    (A) Do not bind to the active site
    (B) Stabilize the enzyme in its R conformation
    (C) Do not inhibit enzyme activity
    (D) Mimic reaction products
    (E) Do not alter reaction kinetics

11. Which is the most accurate description of the fully functional structure of aspartate transcarbamoylase (ATCase)?
    (A) Two trimers connected by 3 dimers
    (B) A tetramer
    (C) A dimer of dimers
    (D) c_3r_2
    (E) $3c_22r_3$

12. During activation of ATCase, conversion from T to R does **NOT** involve the following:
    (A) Separation of catalytic subunits
    (B) Rotation of catalytic subunits
    (C) Rotation of regulatory dimers
    (D) Interactions between regulatory dimers
    (E) Communication between subunits

13. Which of the following proteins and their ligands show positive heterotropic interaction:
    (A) Hemoglobin: H^+
    (B) Hemoglobin: O_2
    (C) Phosphofructokinase-1: AMP
    (D) Phosphofructokinase-1: ATP
    (E) Aspartate transcarbamoylase: CTP

14. Which statement accurately describes the modification of proteins by the cholera toxin:
    (A) It occurs catalytically, outside cells
    (B) It occurs non-catalytically, within cells
    (C) It occurs uniquely to protein kinase A
    (D) It is a form of ATP-dependent phosphorylation
    (E) It is a form of ADP-ribosylation

15. Which of the following accurately completes the sentence? The interactions of ligands with proteins are generally **NOT** _____.

(A) specific
(B) permanent
(C) transient
(D) complementary
(E) any of the above

17. You have just purified a novel, non-enzymatic protein based on its ability to bind to phosphorylated tyrosine residues. This property *suggests* that the protein contains:

(A) A DNA-binding domain
(B) A catalytic serine
(C) An SH3 domain
(D) An SH2 domain
(E) An O_2-binding site

18. In sickle cell anemia, hemoglobin molecules aggregate because of the following:

(A) Valine residues are more hydrophobic than glutamate residues
(B) Glutamate residues are more hydrophobic than valine residues
(C) Hydrophilic interactions
(D) Changes in the conformation of the active site
(E) None of the above

19. Which of the following is **true** concerning the activation of cyclin-dependent kinases?:

(A) Phosphorylation of Tyr-15 repositions the PSTAIRE helix
(B) Phosphorylation of Thr-160 repositions the PSTAIRE helix
(C) Cyclin binding repositions the PSTAIRE helix and exposes Thr160
(D) Cyclin binding repositions the PSTAIRE helix and blocks access to Thr160
(E) Phosphorylated Tyr-15 binds to Arg residues to stabilize the active site

21. In metabolic pathways, the regulated steps are:

(A) Often endergonic

(B) Usually substrate limited

(C) Usually at or near equilibrium

(D) Usually characterized by large positive values of ΔG

(E) Usually characterized by large negative values of ΔG

22. Which of the following steps is rate-limiting during glycolysis:

(A) Conversion of glucose 6-phosphate to fructose 6-phosphate

(B) Conversion of fructose 1,6-bisphosphate to fructose 6-phosphate

(C) Conversion of 3-phosphoglycerate to 2-phosphoglycerate

(D) Conversion of phosphoenolpyruvate to pyruvate

(E) None of the above

23. During gluconeogenesis, which step is highly exergonic:

(A) Conversion of glucose 6-phosphate to fructose 6-phosphate

(B) Conversion of fructose 6-phosphate to fructose 1,6-bisphosphate

(C) Conversion of pyruvate to phosphoenolpyruvate

(D) A and B

(E) B and C

24. Which of the following statements is TRUE of gluconeogenesis:

(A) It can be used to derive glucose from any amino acid

(B) It occurs in neurons

(C) It occurs in liver cells

(D) It occurs completely within mitochondria

(E) It occurs only in adipose tissue

26. There are different isoforms of PFK-2/FBPase-2 expressed in the liver and muscle of many mammals. If the muscle isoform is phosphorylated by PKA:

(A) It is active as fructose 2,6-bisphosphatase

(B) It is likely to use fructose 1,6-bisphosphate as a substrate

(C) The liver isoform is active as phosphofructokinase-2

(D) The liver isoform is likely to use fructose 2,6-bisphosphate as a substrate

(E) The liver isoform is likely to use fructose 6-phosphate as a substrate

27. Which of the following is an allosteric inhibitor of pyruvate kinase:

(A) ADP

(B) Acetyl-CoA

(C) Ribose 5-phosphate

(D) Fructose 1,6-bisphosphate

(E) Fructose 2,6-bisphosphate

28. Which step in glycolysis is regulated by the binding of a regulatory protein:

(A) The step catalyzed by phosphofructokinase-1

(B) The step catalyzed by hexokinase I

(C) The step catalyzed by muscle hexokinase

(D) The step catalyzed by hexokinase IV

(E) The step catalyzed by pyruvate kinase

29. In muscle cells, glycogen phosphorylase is inhibited by glycogen phosphorylase *a* phosphatase. The action of this phosphatase is:

(A) Promoted by binding of glucose to the phosphorylase

(B) Promoted by binding of glucose to the phosphatase

(C) Dependent upon UDP-glucose

(D) Dependent upon glucose 1-phosphate

(E) Needed to produce ATP

30. Glycogen synthase kinase 3 (GSK3) effectively reduces glycogen synthesis by:

(A) Phosphorylating protein kinase A

(B) Phosphorylating glycogen phosphorylase

(C) Dephosphorylating glycogen synthase

(D) Dephosphorylating glycogen phosphorylase

(E) Phosphorylating glycogen synthase

<u>Part II</u>: SHORT ANSWER QUESTIONS 1 - 9 (*30 marks*)

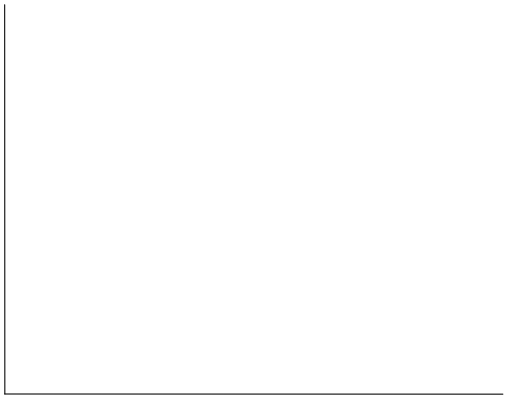
Please answer the following questions in the space provided.

1. Loss of p53 expression promotes the development of malignant tumours. With specific reference to the function of cyclin-dependent kinases, describe how this happens. (*3 marks*)

Part II – cont.

2. A research team working for the Toronto Maple Leafs has engineered a mutant form of hemoglobin (HbML) that is capable of delivering more O_2 to the tissues (e.g. brains) of the Leafs' defencemen. HbML works because it has an altered affinity for 2,3-bisphosphoglycerate (BPG) compared to normal hemoglobin (HbA).

(a) Draw substrate-binding curves for HbML and HbA in the presence of BPG. Put both curves on the same plot. Be sure to label the axes and the curves clearly. (3 marks)



(b) BONUS: Where on HbML did the researchers introduced the mutation? (1 mark)

3. Explain the molecular mechanism by which O_2 binding to hemoglobin induces conformational changes in the protein. (3 marks)

Part II – cont.

4. Write the letter corresponding to one of the terms on the left in the space beside the appropriate phrase in the list on the right. This is complete when each phrase on the right has **one** letter beside it (you will not use every letter on the left). (*4 marks*)

(a) isoleucine 16
(b) His HC3
(c) Glutamate 51
(d) ADP-ribosylation
(e) F8
(f) serine 195
(g) E7

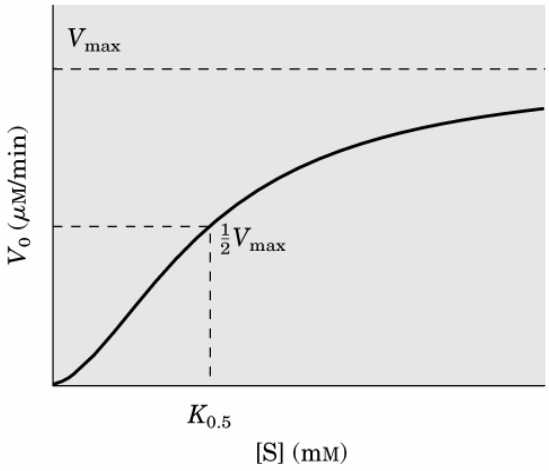
___ distal histidine of hemoglobin
____ ion pair with Lys C5 of hemoglobin
____ ion pair with Asp 194 of chymotrypsin
____ CDK active site

5. Describe the sequence of events that convert fibrinogen into a 'hard' clot during blood clotting. (*3 marks*)

Part II – cont.

6. **(a)** In ATCase, mutation of D236c or K143r to alanine can dramatically alter the behaviour of the enzyme (recall the paper by Stieglitz *et al.*). Exactly, what effect do these mutations have on the structure and function of ATCase? (*3 marks)*

(b) Below is the substrate-activity curve for aspartate transcarbamoylase (ATCase). On the graph, draw the curve for ATCase activity in the presence of ATP. (*1 mark)*



Part II – cont.

7. (a) What amino acids can protein kinase A phosphorylate? (*1 mark*)

(b) Describe how the activity of protein kinase A is regulated. (*3 marks*)

8. The function of some proteins can be altered when the proteins are phosphorylated. List 2 biochemical effects of phosphorylation that could cause altered activity. (*2 marks*)

9. Fructose 2,6-bisphosphate is potent allosteric modulator of glycolysis and gluconeogenesis.

(a) Name the enzymes it modulates directly, and whether it is an activator or inhibitor of the enzyme. (*2 marks*)

(c) How is the concentration of fructose 2,6-bisphosphate controlled reciprocally in liver and muscle cells? (*2 marks*)