IMPERIAL COLLEGE LONDON

B.Sc. Examination 2017

This paper is also taken for the relevant examination for the Associateship of the Royal College of Science

BIOLOGICAL CHEMISTRY

Tuesday 31 January 2017 10.00 - 13.00

FOR FIRST YEAR STUDENTS IN BIOCHEMISTRY AND BIOTECHNOLOGY

Please use the top answer book for Section A and separate answer books for each question in Section B. Parts of a question carry equal weighting unless otherwise specified.

A number of equations from physical chemistry are included at the end of the paper.

SECTION A

ANSWER ALL QUESTIONS. This section is worth 40% of the total marks. Each question is worth 4% of the total marks. Candidates should allow about 70 minutes for this section.

1. Name and draw the structure of each amino acid that has a methyl group ($-CH_3$) attached to the β carbon in the side chain.

2. Draw an energy level diagram for a carbon-carbon double bond and indicate what occurs when light is absorbed by the bond.

3. Major symptoms of glucose 6-phosphatase deficiency are an enlarged liver due to glycogen accumulation and poor tolerance of fasting. Explain the biochemical basis for these symptoms.

4. Which one of the following functional groups can behave as a nucleophile at pH 7: amino group, amide group or thiol group? Explain why the other two are not nucleophilic.

5. For the hydrogen bonds that form in α helices and β sheets, indicate what group is the hydrogen bond donor, what group is the hydrogen bond acceptor and how many hydrogen bonds are formed per amino acid residue.

6. (a) Name one enzyme in the glycolytic pathway and one in the TCA (Krebs) cycle the activities of which are regulated by the levels of available ATP.
   (b) State the components of the proton motive force.

7. Write a balanced equation, including chemical structures, for formation of a peptide bond between tyrosine and serine and indicate what type of reaction this is.

8. For a closed system, heat that enters the system results in an increase in enthalpy of the system. Describe what forms the enthalpy takes for a system consisting of a block of ice that is heated from -20 ºC to +20 ºC.

9. How do NAD^+ and $NADP^+$ differ in structure? What are their functions in metabolism? Describe ***one*** reaction that produces NADPH.

10. Use an appropriate energy diagram to define a steric clash between two atoms.

SECTION B

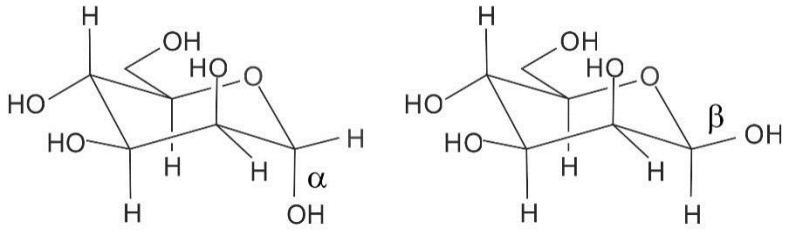
ANSWER FOUR QUESTIONS. This section is worth 60% of the total marks. Each question is worth 15% of the total marks. Candidates should allow about 110 minutes for this section. USE A SEPARATE ANSWER BOOK FOR EACH QUESTION.

11. A biology student makes the claim that 'glycine is a boring amino acid.' Refute this statement with a detailed argument using your biochemical knowledge of why unique properties of glycine are essential in forming specific protein structures such as those found in the fibrous proteins silk fibroin and collagen and in the loops of globular proteins.

12. Give detailed explanations for the following features of stability in biological molecules, reflecting energetically favourable states.

    (a) The *trans* configuration of the peptide bond is more stable than the *cis* configuration.

    (b) The α configuration of mannose is more stable than the β configuration.



    (c) The phosphate ion is very stable compared to phosphate in ester and anhydride linkages.

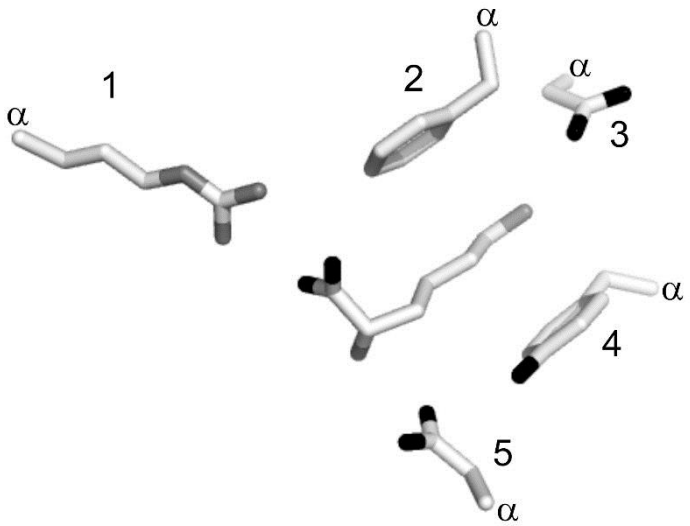
13. Explain the roles of each of the following in glycogen metabolism:

    (a) UDP-glucose

    (b) Cyclic AMP (cAMP)

    (c) Inorganic phosphate (P_i)

14. Periplasmic binding proteins allow bacteria to scavenge for dilute nutrients in the environment. One of the binding proteins is the lysine binding protein, which binds lysine as well as other basic amino acids. The binding site looks like the following, in which the bound lysine is shown along with the α carbon and side chains of amino acid residues from the binding protein that interact with the bound lysine. Carbon atoms are white, nitrogen atoms are grey and oxygen atoms are black; hydrogen atoms are not shown.



(a) Identify the amino acid side chains involved in the binding interaction (15%).

(b) Describe what types of dipole-dipole interactions could form between the protein and ligand (20%).

(c) The following data were obtained for binding of lysine to 1 mg of the binding protein, which has a molecular weight of 27120.

Free lysine concentration (μM)	nmole of bound lysine
0	0.0
5	9.2
10	14.7
20	21.0
40	26.8
60	29.5
80	31.0
100	32.0
120	32.8
140	33.3

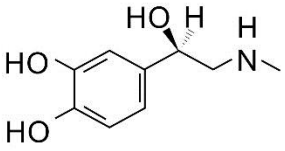
Plot a binding curve showing moles of bound lysine per mole of protein as a function of free lysine concentration (25%).

(d) From your graph, determine the dissociation constant (K_D) for binding of lysine to the binding protein (15%).

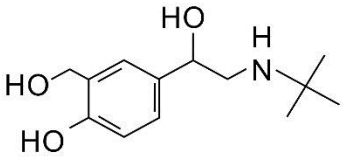
(e) If amino acid 3 is replaced by alanine in a different strain of bacteria, use your knowledge of typical bond energies to estimate how much this would change the K_D for lysine (25%).

15. Salbutamol is a drug used in inhalers to relieve the symptoms of asthma by mimicking the action of epinephrine (adrenaline), binding to β-adrenergic receptors in lung and causing relaxation of the smooth muscles.

Epinephrine (adrenaline)



Salbutamol



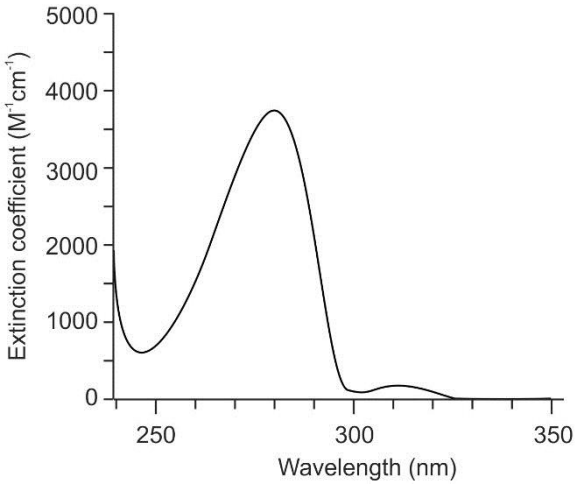
The form of salbutamol used in inhalers is a racemic mixture, meaning that it has equal amounts of two enantiomers.

(a) Explain why there are two enantiomeric forms of salbutamol. [Hint: you need to add the implicit hydrogen atoms to the structure.] (20%)

(b) Draw the structures of the two enantiomers of salbutamol based on the system used in the structure shown for epinephrine. (15%)

(c) Only one of the enantiomers actually binds to the β-adrenergic receptor. Based on a comparison with epinephrine, indicate which of your structures would most likely bind to the receptor. [You do not need to name the structures.] (15%)

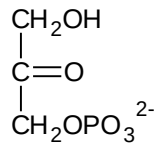
(d) When salbutamol is synthesized and packaged in inhalers, it is necessary to measure its concentration in solution. This is done using a spectrophotometer. Based on the graph below, determine the extinction coefficient for salbutamol at 280 nm. (15%)



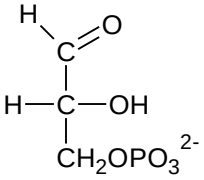
(e) The formulation of salbutamol used in an inhaler is 5 mg / 2.5 ml. Use the extinction coefficient to determine what absorbance at 280 nm you would need in a 1-cm cuvette if you want to achieve this concentration. Based on the result, suggest what you need to do in order to make this measurement. The molecular weight of salbutamol is 239. (35%)

16. (a) With the help of a diagram explain why the alpha carbon of many carbonyl compounds can behave as a nucleophile. (30%)

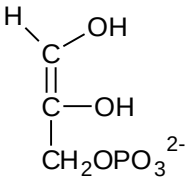
(b) Triose phosphate isomerase catalyses the conversion of dihydroxyacetone phosphate (I) to glyceraldehyde-3-phosphate (II) in the glycolysis pathway. The reaction is thought to proceed via the enediol intermediate (III). All three are isomers. What is the name given to this type of isomer? Using curly arrows show the mechanism for the conversion of (I) to (II) via intermediate (III). Name two amino acids that you would expect to find in the active site of triose phosphate isomerase. Explain your answer. (70%)



(I)



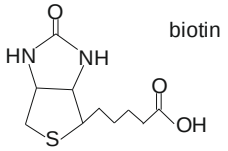
(II)



(III)

17. (a) Early experiments to determine the pathway for fatty acid synthesis showed that bicarbonate (HCO_3^-) is required for the synthesis of palmitate. However, only very low amounts of bicarbonate were found to be needed for palmitate synthesis and there was no correlation seen between the amount of bicarbonate and the amount of palmitate synthesized. In addition, when ^{14}C-labelled bicarbonate was used, no ^{14}C was incorporated into palmitate. Explain these observations.

(b) Explain why deficiency of biotin (vitamin B5 - shown below) would reduce synthesis of glucose by gluconeogenesis and decrease degradation of odd-chain fatty acids as well as reducing synthesis of fatty acids.



18. (a) Explain how ATP, ADP and Pi are transported across the inner mitochondrial membrane. (30%)

(b) Describe, using words and diagrams, the mechanism of ATP synthesis by the rotary ATP synthase enzyme. (70%)

Equations and constants from physical chemistry

Ideal gas law:	$PV = nRT$
Free energy changes:	$\Delta G = \Delta H - T\Delta S$ (at constant temperature)
	$\Delta G = \Delta G° + RT \cdot \ln(\Gamma)$
Chemical potential:	$\mu_A = \mu_A° + RT \cdot \ln[A]$
Relationship of standard chemical potential and equilibrium constant:	$(\Delta\overline{G}°) = \Delta\mu° = - RT \cdot \ln(K_{eq})$
Relationship of oxidation potential and free energy (n = number of electrons):	$\Delta\mathcal{E} = - \Delta G/nF$
Free energy and binding:	$\Delta G°_{Association} = - RT \cdot \ln(K_A) = RT \cdot \ln(K_D)$
Nernst equation (z = charge on ionic species):	$\Delta\Psi = - RT/zF \cdot \ln([A]_{in}/[A]_{out})$
Henderson-Hasselbalch equation:	$pH = pK_a + \log([\text{unprotonated}]/[\text{protonated}])$
Light energy:	$\Delta E = h \cdot \nu = h \cdot c / \lambda$
Beer-Lambert Law:	$A = \varepsilon \cdot c \cdot l$
Coulomb potential:	$E \propto q_1 \cdot q_2 / r$
Gas constant:	$R = 8.314\ J\ mol^{-1}\ K^{-1}$
Faraday:	$F = 96.48\ kJ\ mol^{-1}\ V^{-1}$

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