IMPERIAL COLLEGE LONDON

BSc and MSci DEGREES – MAY 2010, for Internal Students of the Imperial College of Science, Technology and Medicine

This paper is also taken for the relevant examination for the Associateship

ADVANCED CHEMISTRY THEORY IIIB

Paper 1

Tuesday 4th May 2010, 09:30-12:30

USE A SEPARATE ANSWER BOOK FOR EACH QUESTION. WRITE YOUR CANDIDATE NUMBER ON EACH ANSWER BOOK.

3.I5 – Bioinorganic Chemistry

Answer part (a) **AND EITHER** part (b) **OR** part (c)

a)

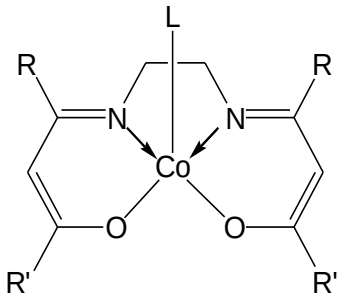
i) Discuss the chemical characteristics of zinc which are important to its catalytic function in biological systems.

(8 marks)

ii) Draw the full catalytic cycle for the hydration of CO_2 by the zinc containing carbonic anhydrase II enzyme.

(5 marks)

b) The cobalt(II) Schiff base complex **A** has been studied as a model for the Fe Haem centres in Myoglobin and Haemoglobin, as it too is able to bind dioxygen reversibly.



A

i) Discuss in detail how O_2 can bond to the cobalt centre in **A**. Include in your answer a full description of the molecular orbitals involved, and of any electron transfer processes.

(5 marks)

ii) Why is the presence of a strongly coordinating axial ligand L in **A** important in allowing facile O_2 binding to occur?

(5 marks)

iii) IR or Raman spectroscopy is commonly used to monitor the bonding of O_2 to complexes such as **A**. What changes on O_2 binding would you expect to see using these spectroscopic techniques and why?

(2 marks)

QUESTION CONTINUED OVERLEAF

c)

i) Briefly describe or illustrate the coordination sphere of the two copper centres in the deoxy form of Haemocyanin. State the oxidation state of the copper centres in this deoxy form and their d-electron count.

(2 marks)

ii) Describe how dioxygen can bind to Haemocyanin. Include in your answer a full description of what orbitals are used on both the dioxygen and copper centres and discuss any electron transfer process.

(5 marks)

iii) Spectroscopic studies of oxy-haemocyanin show several salient features: Infrared spectroscopy shows an absorption at 755 cm^{-1}; UV-Vis spectroscopy shows very intense absorbances at 350 and 580 nm; no EPR spectrum is observed (oxyhaemocyanin is EPR-silent). Suggest explanations for these spectroscopic observations.

(5 marks)

3.O2 – Biological Chemistry

Answer **EITHER** part a) **OR** part b)

a) Answer **ALL** parts of this question.

i) Draw the four main "building blocks" for the primary structure of DNA.

(7 marks)

ii) Single DNA polydeoxynucleotide chains have considerable restrictions with respect to their conformational flexibility. Explain these restrictions in detail.

(10 marks)

iii) Suggest how you think that these restrictions could be considered ideal for double helix formation.

(8 marks)

b) Answer **ALL** parts of this question.

i) Explain in outline how you might obtain protein crystals for X-ray crystallography.

(7 marks)

ii) Outline the principles of X-ray crystallography for protein structure determination. Your answer should include a description of the unit cell, diffraction planes and the vector model of diffraction.

(10 marks)

iii) What do you think might be the limitations of this technique for accurate structure and function determination?

(8 marks)

3.O7 – Polymers

Answer part (a) and **EITHER** part (b) **OR** part (c).

a) Answer **ALL** parts

i) Give a brief definition of the following terms:
anneal
tacticity
void volume

(3 marks)

ii) Why does the addition of alumina (as AlO_4) tetrahedra into a silica glass network increase the glass transition temperature, Tg?

(2 marks)

iii) Explain what Ostwald ripening is. What force drives this process?

(2 marks)

iv) Explain what is meant by radius of gyration.

(2 marks)

v) What is the relationship between molecular weight and glass transition temperature, Tg? Sketch a graph for this.

(2 marks)

vi) Explain what a Flory or θ solvent is.

(2 marks)

vii) What is free volume?

(2 marks)

b) Answer **ALL** parts

i) Describe how the glass transition temperature, Tg, may depend upon the Q structure of a glassy silicate polymer. Explain why a glass, a Q_2 silicate chain, crystallises more rapidly than a Q_4 silicate. Illustrate your answer with examples of each.

(5 marks)

ii) Explain the factors that cause line broadening in the X-ray diffraction of polymers.

(5 marks)

QUESTION CONTINUED OVERLEAF

c) Answer **ALL** parts

i) What are plasticisation and anti-plasticisation? Give examples of each.

(5 marks)

ii) A commonly used dental polymer is cured using ultra-violet light. Exposure to the u-v light causes a rapid increase in viscosity, however over exposure causes embrittlement. Explain both of these observations.

(5 marks)

3.P4 – Introduction to Molecular Biophysics

Answer part (a) and **EITHER** part (b) **OR** part (c).

a) Answer **ALL** parts of this question

i) Describe briefly how the complementarity of base pairs determines DNA structure, and storage and processing of genetic information.

(5 marks)

ii) How many charges does a fully dissociated 1 μm long double strand DNA molecule have? Take the helical pitch as 3.4 nm.

(3 marks)

iii) Describe the factors that prevent DNA aggregation and explain how DNA packing and condensation can be induced without histones.

(2.5 marks)

iv) Explain which forces a molecular motor will have to work against in packing DNA into a bacteriophage capsid.

(2 marks)

b) Answer **ALL** parts of this question

i) What is the difference between protein melting and protein unfolding?

(1 mark)

ii) ***Zimm-Bragg theory*** of protein melting provides the portion, θ ,of intact bonds in a long alpha-helical or beta-sheet polypeptide chain given by the expression

$$\theta = \frac{1}{2}\left\{1 - \frac{1-s}{\sqrt{4\sigma s + (1-s)^2}}\right\}$$

where s is the chain ***stability parameter***, and σ is the ***cooperativity parameter***. Explain the physical meaning of these parameters and give their definitions in terms of the corresponding free energies.

(3.5 marks)

iii) Is protein melting a true phase transition? How is the transition temperature defined?

(2 marks)

iv) Consider a protein solution at room temperature in which breaking a hydrogen bond in a long β-sheet costs 0.05 eV of free energy. Using Zimm-Bragg theory estimate the ***average portion of broken bonds***, given the cooperativity cost (free energy increase per melted section) to be equal to 0.06 eV.

(3 marks)

QUESTION CONTINUED OVERLEAF

v) Estimate the ***average portion of broken bonds*** if the temperature is increased to 55˚C and at this temperature the cost of breaking a hydrogen bond becomes only 0.01 eV (assume the cooperativity cost remains the same).

(3 marks)

c) Answer **ALL** parts of this question

i) Consider the density of negative charge of different species in the *interior* of a cell to be equivalent to 0.125 M of excess electrons, and the average concentrations of Na^+ , K^+ , and Cl^- in the *exterior* of the cell to be $c_{Na^+,1} = 0.14\,\text{M}$, $c_{K^+,1} = 0.01\,\text{M}$, $c_{Cl^-,1} = 0.01\,\text{M}$.

Using the electroneutrality condition inside the cell and the equations of Nernst equilibrium, calculate the sodium ion concentration inside the cell and the corresponding equilibrium Nernst potential.

[Hint: use the fact that at equilibrium the Nernst potential is the same for all three ions].

(3.5 marks)

ii) Compare your result with the experimental values in the table below. Explain the discrepancy and discuss the sodium anomaly.

(2 marks)

ion	valence z	interior $c_{2,i}$, mM	relation	exterior $c_{1,i}$, mM	Nernst potential $\mathcal{V}_i^{\text{Nernst}}$, mV
K^+	+1	400	>	20	−75
Na^+	+1	**50**	<	**440**	**+54**
Cl^-	−1	52	<	560	−59

iii) Why is the equilibrium Nernst potential the same for all ions, but the experimentally determined Nernst potentials are ion dependent?

(1 mark)

iv) Describe the origin of the resting potential and explain the difference between ***passive*** and ***active transport*** of ions through ion channels?

(1.5 marks)

v) Compare the free energy gain from hydrolyzing one ATP molecule ($19k_BT$) with the estimated work of running the Na^+/K^+ pump through one cycle (i.e. transferring one Na^+ and one K^+ ion). Take the resting potential as -60 mV.
[Hints: you will need to calculate
1) the work of transferring one sodium ion against the resting potential and the change in entropy due to this act, reflected by its nonequilibrium Nernst potential;
2) the same quantities need to be calculated for the potassium ion;
3) the corresponding Nernst potentials are given in the Table above]

(4.5 marks)

3.P7 – Lyotropics

Answer any **TWO** of the three parts a), b) and c)

a) Answer **ALL** parts of this question.

The thermodynamics of amphiphile aggregation into micelles is described by:

$$\left(\mu^{\circ}_{mic,m} - \mu^{\circ}_{1}\right) = RT \ln x_1 - \frac{RT}{m} \ln\left(\frac{x_m}{m}\right)$$

i) Define m, x_1, and x_m.

(1.5 marks)

ii) Describe what $\left(\mu^{\circ}_{mic,m} - \mu^{\circ}_{1}\right)$ represents, and describe briefly the four main contributions to it.

(3 marks)

iii) Rearrange the above equation into a distribution function for micelle size.

(5 marks)

iv) Deduce how $\mu^{\circ}_{mic,m}$ must vary with increasing m in order for aggregation to occur.

(3 marks)

b) Answer **ALL** parts of this question.

For a curved interface, the cross-sectional area depends on the distance d moved perpendicular to the interface. The result from geometry is:

$$a(d) = a_o\left[1 + 2Hd + Kd^2\right]$$

where we take the positive d-direction to be moving from the hydrocarbon chain end towards the polar headgroup.

i) Name H and K, and define them.

(3 marks)

ii) Calculate H and K for a spherical micelle of radius R, a long cylindrical micelle of radius R, and an inverse spherical micelle of water core radius R.

(3 marks)

QUESTION CONTINUED OVERLEAF

iii) Calculate the area per molecule at the surface of a spherical micelle of *hydrophobic* radius R = 2 nm, if a_0 = 0.45 nm^2 is the value at the polar-nonpolar interface. Assume the polar headgroup region is 0.5 nm thick.

(3 marks)

iv) A lipid bilayer of thickness d_b = 5 nm is draped onto a saddle surface with principal curvatures $c_1 = -c_2 = 0.09$ nm^{-1}. Calculate the headgroup area per lipid molecule if the area per molecule at the bilayer mid-plane is a_o = 0.70 nm^2.

(3.5 marks)

c) Answer **ALL** parts of this question.

When a lipid bilayer vesicle is sucked into a micropipette, the change in membrane area is given by:

$$\Delta A = 2\pi R_p \left(1 - \frac{R_p}{R_s}\right) L_p$$

i) Define R_s, R_p and L_p, and indicate them on a sketch of the vesicle / pipette system.

(2.5 marks)

ii) Calculate ΔA when a 50 micron diameter vesicle is sucked a distance of 15 microns into a micropipette of inner diameter 5 microns.

(1.5 marks)

iii) By equating the work done (force x distance) by a suction pressure Δp in pulling the vesicle partially into the micropipette, with $\sigma \Delta A$ (the applied tension, σ, times the total change in membrane area of the vesicle), show that:

$$\sigma = \frac{\Delta p}{2}\left(\frac{R_p}{1 - R_p / R_s}\right)$$

(4 marks)

iv) Hence calculate σ for the vesicle in part (ii), if a suction pressure of 10^4 Pa was applied.

(2 marks)

v) Hence calculate K_A for the vesicle.

Hint: $\sigma = K_A \alpha$, where α is the area dilation of the vesicle.

(2.5 marks)