IMPERIAL COLLEGE LONDON

BSc and MSci DEGREES – MAY 2011, 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

Monday 9th May 2011, 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** c) of this question.

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

i) Briefly describe or illustrate the coordination sphere of the iron centre in the haem ring of the deoxy form of Haemoglobin and Myoglobin. State the oxidation state of the iron in this deoxy form, and draw its d-electron configuration.

(4 marks)

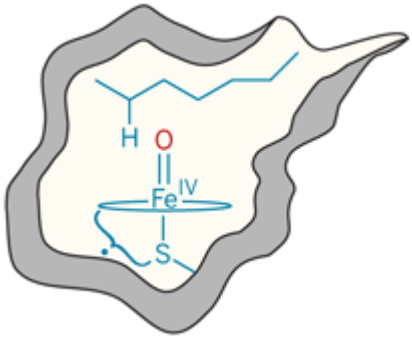
ii) Describe how dioxygen can bind to the iron centre in Myoglobin. Include in your answer a full description of the orbitals which are used on both the dioxygen and iron centre and discuss any changes in the d-electron configuration of the iron.

(6 marks)

iii) Briefly discuss the *allosteric* (co-operative O_2 binding) effect in Haemoglobin.

(3 marks)

b) A key breakthrough in the understanding of cytochrome P450 enzymes was recently reported (J. Rittle and M. T. Green, *Science* 2010, **200**, 933) in which an important reaction intermediate was fully characterised for the first time. A schematic diagram of this intermediate ("Compound I") complete with a bound substrate is shown below.



"Compound I"

i) Briefly discuss the type of reactions catalysed by cytochrome P-450 enzymes. Include in your answer a balanced equation of a representative reaction.

(3 marks)

ii) Discuss the key features of Compound I as shown in the schematic above.

(3 marks)

QUESTION CONTINUED OVERLEAF

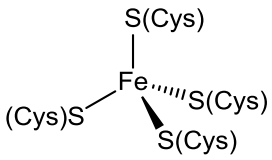
iii) Draw a similar schematic diagram for the next step of the catalytic cycle formed from the rearrangement of Compound I.

(3 marks)

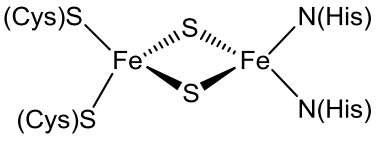
iv) The low temperature electronic structure of Compound I was determined using EPR spectroscopy to reveal a complex pattern described as arising from the exchange coupling of a $S = 1$ and a $S = 1/2$ unit. Suggest the identity of these two units giving your reasoning.

(3 marks)

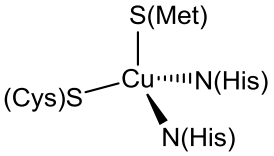
c) Three different catalytic metal centres found in biological electron-transfer proteins are shown below (charges not shown):



A



B



C

i) Draw the redox half-equations for each of **A**, **B** and **C** which occur under physiological conditions.

(3 marks)

ii) Observed μ_{eff} values for the oxidised and reduced form of **B** are 0 and 1.7 BM respectively. Explain these data using d-electron splitting diagrams as part of your answer.

(4 marks)

iii) The protein Plastocyanin contains metal centres similar to type **C** shown above. Discuss what factors facilitate fast electron transfer processes in proteins, with particular reference to Plastocyanin.

(5 marks)

3.O2 – Biological Chemistry Part 2

Answer **EITHER** part a) **OR** part b) of this question.

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

i) Proteins fold much faster than can be achieved by a search of all possible conformations. Explain how this happens.

(6 marks)

ii) Starch and cellulose are plant polysaccharides and are both made up of 1,4-linked glucose units. Account for the observation that despite this similarity starch is used as an energy storage molecule whilst cellulose is a structural molecule.

(6 marks)

iii) When double stranded DNA is heated the two strands separate and the temperature at which this occurs is often referred to as the melting temperature (T_m). The melting temperatures for 2 oligonucleotides are given below:

$(dC)_{10}$:$(dG)_{10}$ 40 $^{\circ}$C
$(dA)_{10}$:$(dT)_{10}$ 20 $^{\circ}$C

Account for the difference in melting temperatures.

(6 marks)

iv) The binding of maltose to the bacterial periplasmic binding protein was investigated by isothermal titration calorimetry and the following results obtained at 25 $^{\circ}$C:

Stoichiometry 1 maltose bound per protein molecule
$\Delta H^{\ominus}$ +38.5 kJ mol^{-1}
K_a 6x10^5 M^{-1}

Using these data calculate the standard Gibbs free energy and entropy. From your calculations identify the driving force for maltose binding and suggest a plausible reason to account for this.

(7 marks)

QUESTION CONTINUED OVERLEAF

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

i)

1. What is the route of information flow from gene to protein in biology?
(3 marks)

2. Why is a triplet code needed in converting a gene sequence to a protein sequence and what is one consequence of this?
(4 marks)

3. In the structure of t-RNA what are the functions of the acceptor stem and the anticodon loop?
(3 marks)

4. How do molecular chaperones act to prevent protein misfolding during protein biosynthesis?
(3 marks)

ii) Protein-ligand interactions involve several types of intramolecular force to achieve both the desired affinity and specificity. Illustrate this statement with respect to the following examples of protein-ligand interaction:

1. Heparin-Antithrombin III.
(4 marks)

2. DNA- Catabolite Repressor Protein (CRP).
(4 marks)

3. The lipid bilayer with Aquaporin.
(4 marks)

3.O7 – Polymers

Answer part a) and **EITHER** part b) **OR** part c) of this question.

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

i) Give a brief definition of the following terms:
- Debye-Scherrer effect
- Paracrystallinity
- tacticity

(3 marks)

ii) What is Rotational Isomeric State theory? How does it apply to polymers?

(3 marks)

iii) Give three physical properties of amorphous materials.

(3 marks)

iv) What is spinodal decomposition?

(3 marks)

v) Explain what the term "fragility" means in relation to glasses.

(3 marks)

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

i) Describe how the crystallisation process can occur in polymers. How does this process start and how can the kinetics be described?

(5 marks)

ii) Describe how solid state NMR spectroscopy can be used to determine the degree of crystallinity in a semi-crystalline polymer?

(5 marks)

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

i) After addition of a small amount of arsenic to molten selenium a dramatic increase in viscosity is observed. Explain this observation. What experiment could you suggest that would verify your hypothesis?

(5 marks)

ii) Describe the salient feature of a radial distribution function with particular reference to amorphous materials and how do they compare to crystalline materials?

(5 marks)

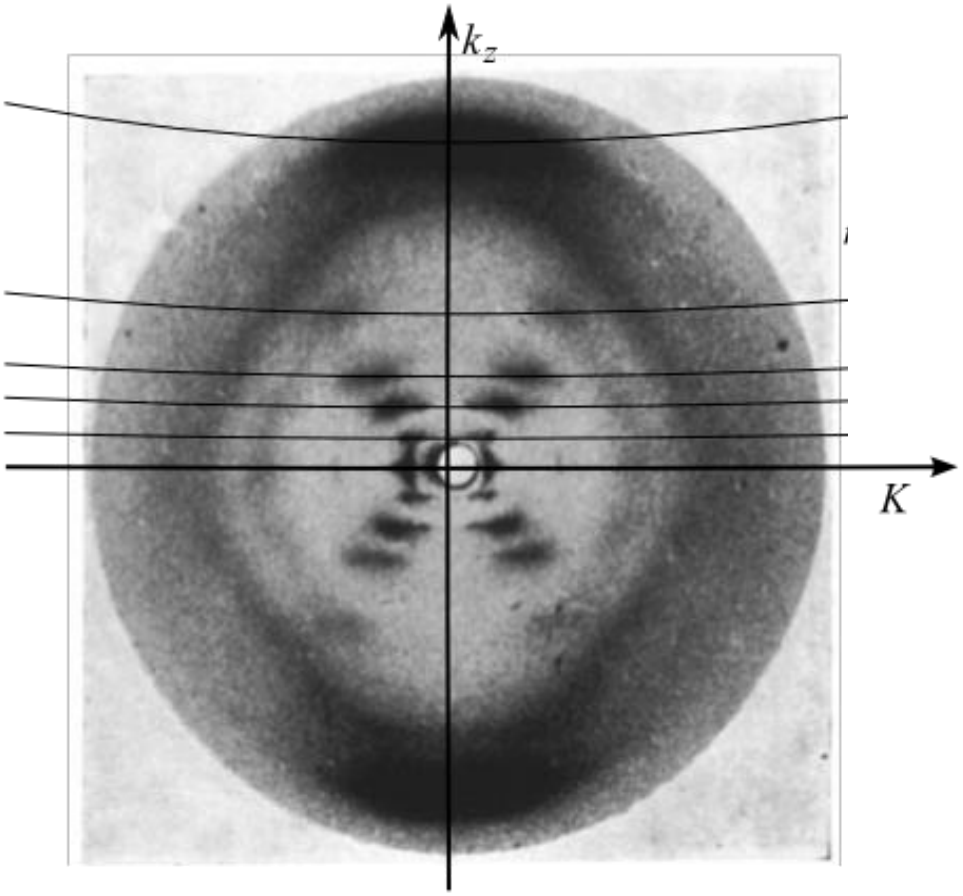
3.P4 – Introduction to Molecular Biophysics

Answer part a) and **EITHER** part b) **OR** part c) of this question.

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

The classical X-ray diffraction pattern for ordered DNA fibres (Franklin and Gosling, 1953), which helped to unravel the structure of DNA, was first interpreted using the CCV –equation [Cochran, Crick, and Vand (1952)].

$$I(\mathbf{k}) \propto N \sum_{n,j=-\infty}^{\infty} \delta_{k_z,\, n\frac{2\pi}{H} - j\frac{2\pi}{h}} \cos^2\left(n\tilde{\phi}_s\right) J_n^2(Ka) + \delta_{k_z,0} J_0^2(Ka) \sum_{\nu \neq \mu} \left\langle e^{i\mathbf{K}\left(\mathbf{R}_\nu - \mathbf{R}_\mu\right)} \right\rangle ;$$



i) Explain each of the terms in this equation.

(4 marks)

ii) Describe the main assumptions and approximations used to derive this equation.

(2.5 marks)

QUESTION CONTINUED OVERLEAF

Evaluate from the X-Ray diffraction pattern the DNA's:

iii) helical pitch

(4.5 marks)

iv) helical rise

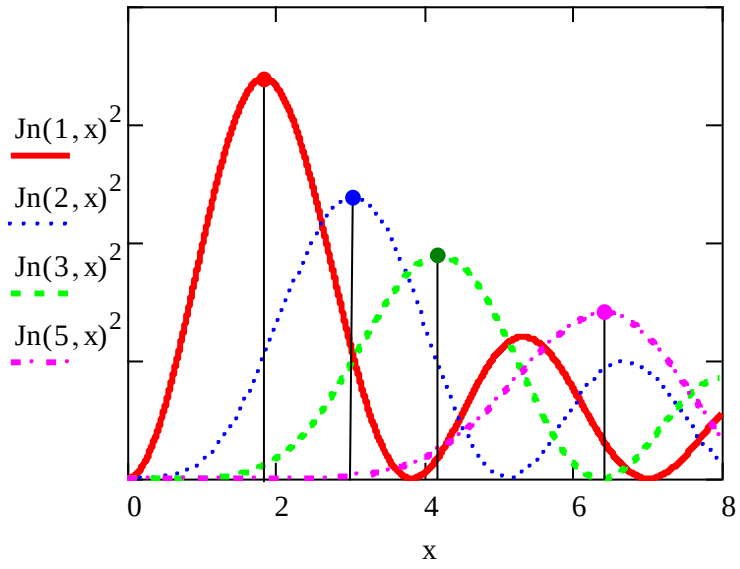
(3 marks)

v) azimuthal width of the minor groove

(2 marks)

Hint: to set a scale on your figure, which has not been shown in the figure above assume that the DNA radius $a \approx 1\text{nm}$ and use the data information for the square of the *Bessel function* drawn below, in which vertical bars show the positions of the first maxima.

$\text{Jn}(n,x) \equiv J_n(x)$ – Bessel function of order n



vi) Why are the spots at high k_z blurred?

(1 mark)

QUESTION CONTINUED OVERLEAF

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

The Chippendale Mupp, a creature of fiction, has a very long tail and a smart tail-based alarm-clock system: before it goes to sleep it bites the end of its tail, so that the nerve impulse triggered by the bite reaches its brain after a certain number of hours.

Two Mupps, father and son, prepare to go to sleep at the same time. In the morning the younger Mupp will have to go to school and they cannot get up late. The Father has a tail 8 times longer than his son and an axon radius 16 times larger. The axon of the tail of the young Mupp has a specific conductivity 4 times higher than the tired axon of the adult Mupp.

i) Which of the two Mupps will wake up earlier and what would be the ratio of their 'sleeping times' if they bite at the very end of their tails?

(5 marks)

ii) How can the 'longer sleeping Mupp' rest his alarm clock to wake up at the time with the other Mupp?

(3 marks)

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

i) Explain qualitatively how the perfect S-rachet model of a molecular motor works and what is the molecular analog of the energy quantum released at each step.

(2 marks)

The speed of motion of a molecular motor which follows the Smoluchowski kinetics of an S-ratchet under a load is given by

$$V = \left[\frac{fL}{k_B T}\right]^2 \frac{D}{L} \frac{1}{e^{\frac{Lf}{k_B T}} - 1 - \frac{fL}{k_B T}}$$

ii) Explain all symbols in this equation.

(1.5 marks)

iii) Derive an expression for the activation energy of speed in the limit of a *heavy* load, assuming that the diffusion constant has an Arrhenius temperature dependence.

(2 marks)

iv) Consider the case when the work against the load in one step has a value of $3k_BT$. How does the speed change when the weight of the load is doubled?

(2.5 marks)

3.P7 – Lyotropics

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

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

The free energy per mole of amphiphile in a micelle of aggregation number *m* may be written:

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

i) Explain what the second term on the right hand side represents.

(1.5 marks)

ii) What is the quantity (x_m/m)?

(1 mark)

iii) Explain why there is a factor of (1/*m*) in front of the ln term.

(1.5 marks)

iv) Write down the equation for the molar free energy μ_w of the monomeric amphiphile in water, defining all terms.

(2 marks)

v) Hence derive an equation for the free energy of formation $\left(\mu^{\circ}_{mic,m} - \mu^{\circ}_{w}\right)$ of micelles of aggregation number *m*.

(2.5 marks)

vi) What is the limiting value of the free energy of formation, as the aggregation number *m* tends to infinity?

(1.5 marks)

vii) Explain how you expect the free energy of micellization to vary with chain length.

(2.5 marks)

QUESTION CONTINUED OVERLEAF

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

A simplified equation for the free energy per molecule in a fluid lipid bilayer is:

$$f_h = \gamma a + \frac{c}{a}$$

i) Define all three terms on the right hand side of this equation.

(1.5 marks)

ii) Sketch f_h versus the surface area per lipid molecule, indicating any important features of the plot.

(2 marks)

iii) Derive an expression for the minimum value of f_h in part (ii).

(2 marks)

iv) Derive an expression for the value of the optimal area per molecule.

(2 marks)

v) Using estimated values of γ = 30 mN m^{-1}, and c = 1 x 10^{-20} J nm^2, for a dialkyl phospholipid, calculate the optimal area per molecule, and explain whether your value of area is physically sensible.

(2.5 marks)

vi) Derive an expression for the lateral repulsion, π, from the equation for f_h, and calculate its value at the optimal area per molecule as calculated in part (v).

(2.5 marks)

QUESTION CONTINUED OVERLEAF

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

The curvature elastic energy per unit area of a thin membrane is given by:

$$g_c = 2\kappa\left(H - H_o\right)^2 + \kappa_G K$$

i) Describe each term on the right hand side of this equation.

(2.5 marks)

ii) Write down equations defining *H* and *K*.

(2 marks)

iii) What does the equation for g_c reduce to, for a long cylindrical membrane of radius *r*?

(1.5 marks)

iv) Prove that the total curvature energy G_c for a spherical, symmetric bilayer vesicle is independent of vesicle radius *R*.

(5 marks)

v) For a symmetric bilayer, what is the relationship between the monolayer values κ^m and H_o^m, and their corresponding bilayer values, κ^b and H_o^b?

(1.5 marks)