THE UNIVERSITY OF MANITOBA

April 23, 2001 FINAL EXAMINATION

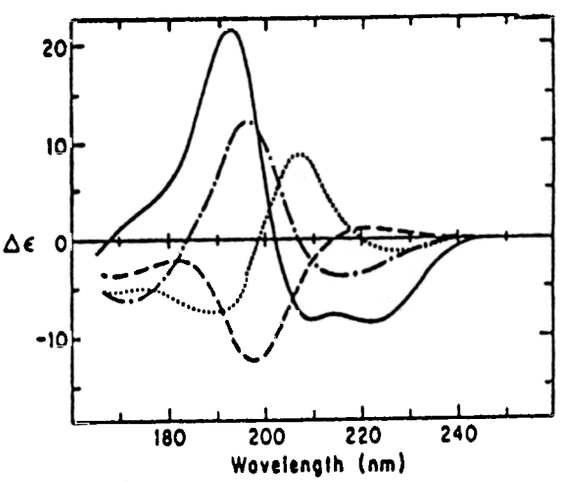
PAPER NO: 611 LOCATION: Fr. Kennedy Brown PAGE NO: 1 of 5

DEPARTMENT & COURSE NO: Chemistry 2.463 TIME 3 HOURS

EXAMINATION: Biochemistry of Proteins EXAMINER: J. O'Neil

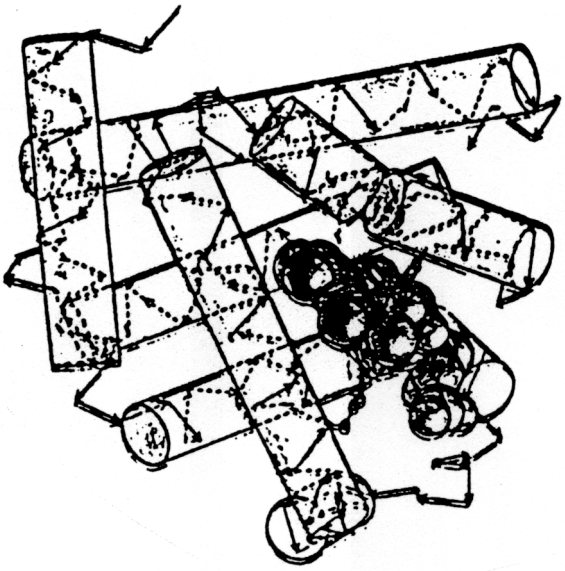
Section 1: *You must answer all of the following questions in* Section 1. *As a guide you can spend up to 2 hours and 20 minutes on this part of the exam. Wherever possible* ***use diagrams*** *to enhance your answers.*

Marks		
8	1	Describe how combinatorial chemistry based on solid-phase peptide synthesis is used in drug discovery.
12	2	With the use of the following diagram explain how circular dichroism spectropolarimetry is used in the analysis of protein structure. Explain the conclusions reached about the structure of the all *D*-amino acid HIV-1 protease based on circular dichroism spectra.



6	3	Draw the chemical structure of the tripeptide Ile-Gly-Arg at pH 7 and label all the dihedral angles with Greek letters or names.
6	4	A π-helix can be designated 4.4_{16}. Using words and diagrams describe the structural properties of the π-helix. How many turns of helix are there in one repeat of the helix? How many residues per repeat? If the rise of the helix is 1.2Å what is the repeat of the helix? What is the pitch?
12	5	Compare and contrast the structural properties of the α-helix and the 3_{10} helix.
10	6	What information did V. N. Ramachandran use to construct his Plot? Draw a Ramachandran Plot and label the locations of the right and left-handed α-helices, parallel and antiparallel β-sheets, the right-hand 3_{10} helix, and the collagen triple helix.
6	7	Using a diagram describe the features of the coiled-coil motif including its helix-packing interactions. Name 1 protein which adopts this structure.

6 8 With the use of the diagram below describe the "globin fold".



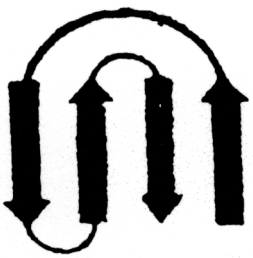
8 9 Prostaglandin H2 synthase-1 is thought to reside in only 1 leaflet of the membrane bilayer. Describe the protein domain which anchors this protein in the leaflet. Name 1 drug molecule that inhibits 1 of the enzymatic activities of this enzyme. Explain why this molecule is a target for the design of new drugs for cancer prevention.

6 10 X-ray diffraction enables the determination of three-dimensional structures of proteins. Explain how the quality of the structures is reflected in the "resolution" and "R-factor" parameters where $R = \Sigma||Fobs|-|Fcalc||/\Sigma|Fobs|$

6 11 Explain the following equation: $RMS = \sqrt{\{[\Sigma_n (r_i-r_j)^2/n]\}}$

6 12 Identify the following structures. What are the main features of each?

A



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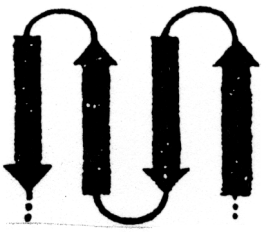


4 13 What is known about the β-sheet propensities of the amino acids?

4 14 Describe the interaction between the signal transduction GTP-binding protein $p21^{ras}$ and membranes and include in your answer a discussion of the pharmaceutical applications of this interaction.

4 15 Describe the homeodomain motif. What is its biological function?

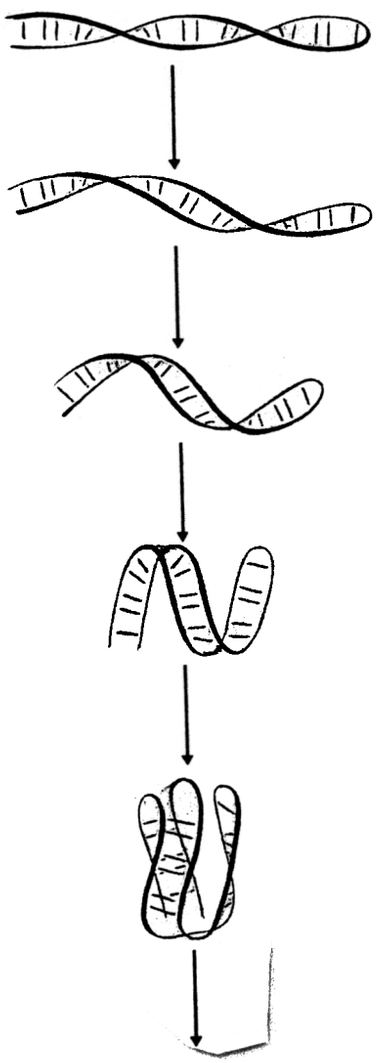
2 16 How many different conformations can a 4 amino acid peptide adopt if each amino acid can adopt 9 different conformations?

Section 2: *Answer 1 of the following questions in* Section 2. *You can spend about 20 min. on this question.*

16 17. Cells have evolved a number of mechanisms to assist protein folding. Describe 6 such mechanisms and name the factors involved in the process.

16 18. Incorporate the following diagrams into a discussion of the structure, function, and pharmaceutical applications of the spherical virus coat proteins.

A



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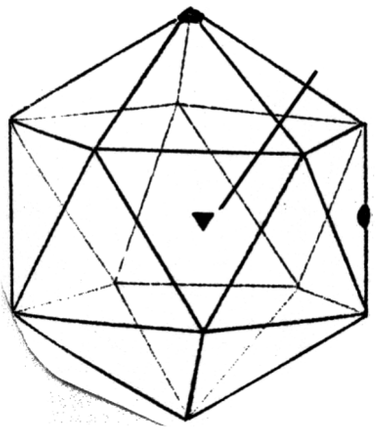

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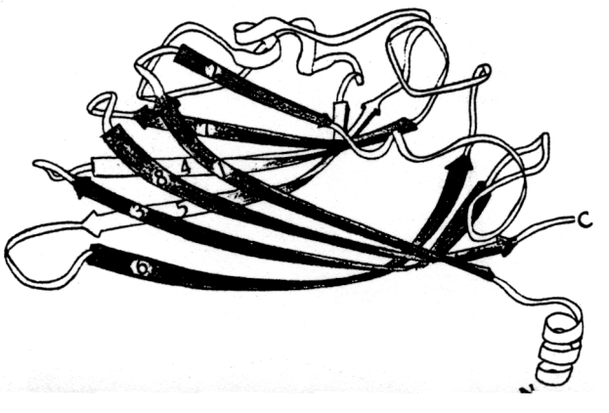
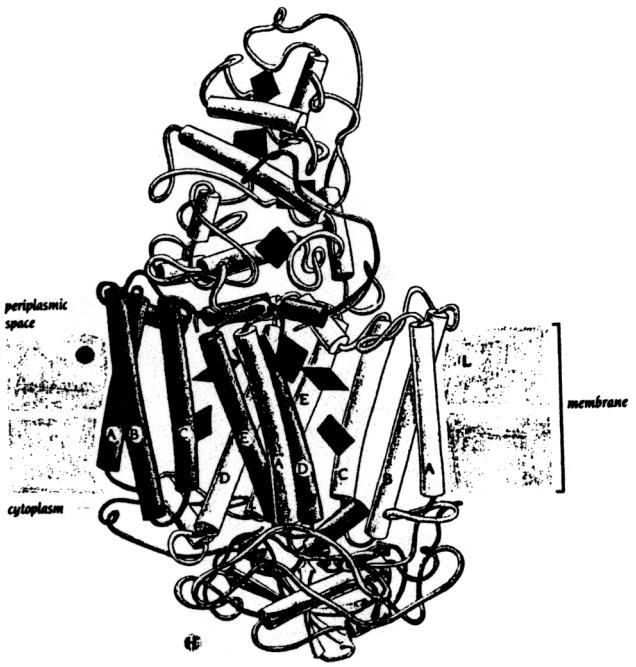


16 20 With the use of the diagrams below discuss the structure of the *Rhodopseudomonis viridis* photosynthetic reaction centre and indicate how knowledge of the structure improves our understanding of the function of the molecule.

A



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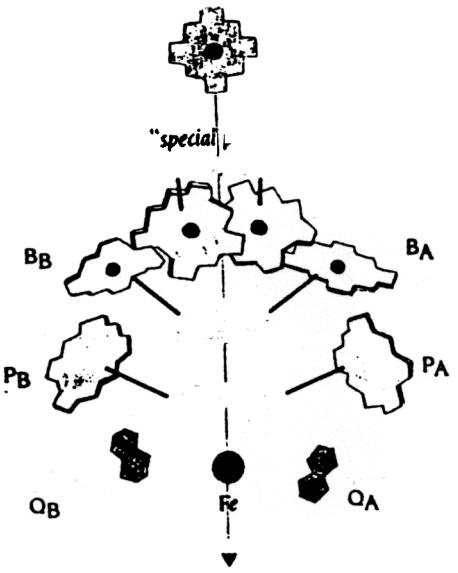

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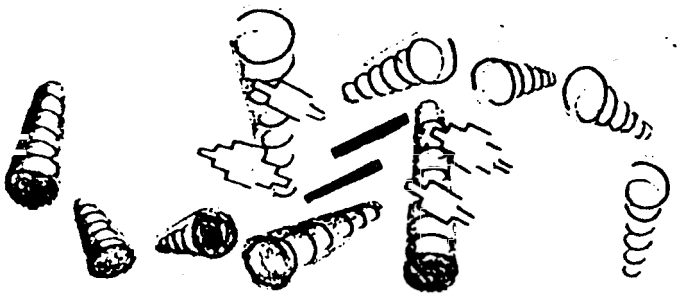

Section 3: *Answer 1 of the following questions in* Section 3. *You can spend about 20 min. on this question.*

16 19. With the use of the diagrams below discuss the structure of the *E. coli* porin complex and indicate how knowledge of the structure improves our understanding of the function of the protein.

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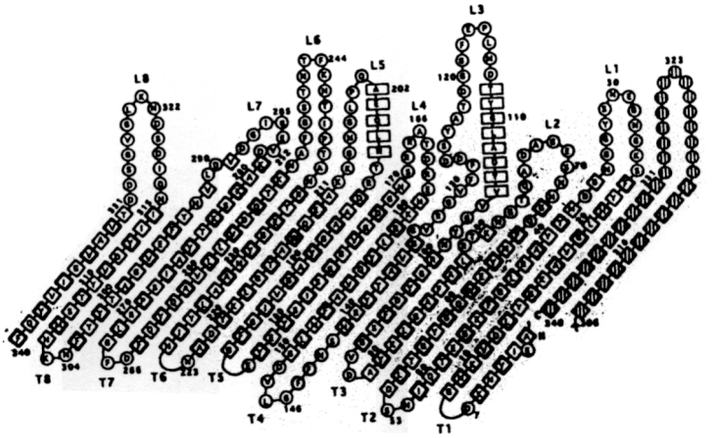

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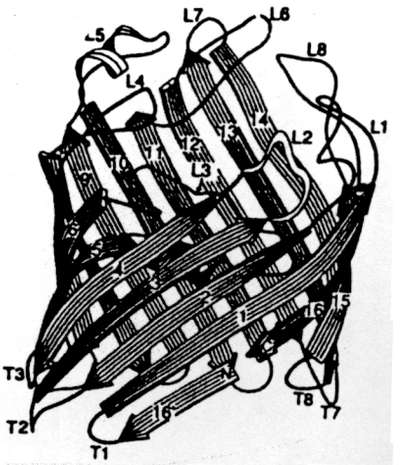

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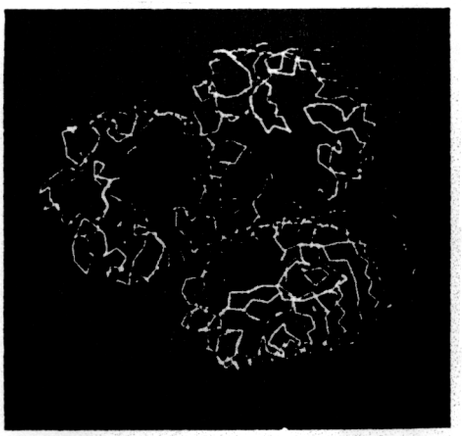

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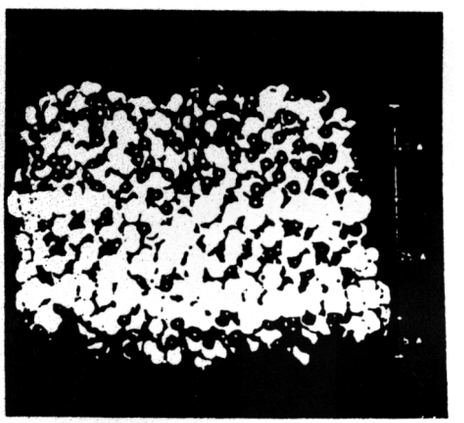

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